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(54) Title: COMPOSITIONS AND METHODS FOR THE THERAPY AND DIAGNOSIS OF PROSTATE CANCER
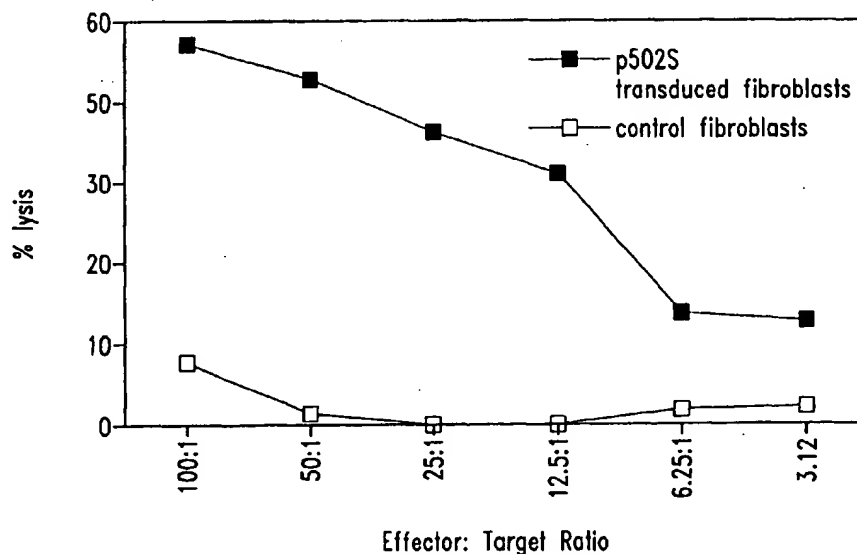
(57) Abstract: Compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer, are disclosed. Compositions may comprise one or more prostate-specific proteins, immunogenic portions thereof, or polynucleotides that encode such portions. Alternatively, a therapeutic composition may comprise an antigen presenting cell that expresses a prostate-specific protein, or a T cell that is specific for cells expressing such a protein. Such compositions may be used, for example, for the prevention and treatment of diseases such as prostate cancer. Diagnostic methods based on detecting a prostate-specific protein, or mRNA encoding such a protein, in a sample are also provided.

COMPOSITIONS AND METHODS FOR THE THERAPY AND
DIAGNOSIS OF PROSTATE CANCER

5   TECHNICAL FIELD

The present invention relates generally to therapy and diagnosis of cancer, such as prostate cancer. The invention is more specifically related to polypeptides comprising at least a portion of a prostate-specific protein, and to polynucleotides encoding such polypeptides. Such polypeptides and polynucleotides may be used in vaccines and pharmaceutical compositions for

10   prevention and treatment of prostate cancer, and for the diagnosis and monitoring of such cancers.

BACKGROUND OF THE INVENTION

Prostate cancer is the most common form of cancer among males, with an estimated incidence of 30% in men over the age of 50. Overwhelming clinical evidence shows that human prostate cancer has the propensity to metastasize to bone, and the disease appears to progress

15   inevitably from androgen dependent to androgen refractory status, leading to increased patient mortality. This prevalent disease is currently the second leading cause of cancer death among men in the U.S.

In spite of considerable research into therapies for the disease, prostate cancer remains difficult to treat. Commonly, treatment is based on surgery and/or radiation therapy, but

20   these methods are ineffective in a significant percentage of cases. Two previously identified prostate specific proteins - prostate specific antigen (PSA) and prostatic acid phosphatase (PAP) - have limited therapeutic and diagnostic potential. For example, PSA levels do not always correlate well with the presence of prostate cancer, being positive in a percentage of non-prostate cancer cases, including benign prostatic hyperplasia (BPH). Furthermore, PSA measurements correlate

25   with prostate volume, and do not indicate the level of metastasis.

In spite of considerable research into therapies for these and other cancers, prostate cancer remains difficult to diagnose and treat effectively. Accordingly, there is a need in the art for improved methods for detecting and treating such cancers. The present invention fulfills these needs and further provides other related advantages.

30   SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compositions and methods for the

diagnosis and therapy of cancer, such as prostate cancer. In one aspect, the present invention provides polypeptides comprising at least a portion of a prostate-specific protein, or a variant thereof. Certain portions and other variants are immunogenic, such that the ability of the variant to react with antigen-specific antisera is not substantially diminished. Within certain embodiments,

5   the polypeptide comprises at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of: (a) sequences recited in any one of SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382,384-476, 524, 526, 530, 531, 533, 535 and 536; (b) sequences that hybridize to any of the

10 foregoing sequences under moderately stringent conditions; and (c) complements of any of the sequence of (a) or (b). In certain specific embodiments, such a polypeptide comprises at least a portion, or variant thereof, of a protein that includes an amino acid sequence selected from the group consisting of sequences recited in any one of SEQ ID NO: 112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534, 537-550.

15   The present invention further provides polynucleotides that encode a polypeptide as described above, or a portion thereof (such as a portion encoding at least 15 amino acid residues of a prostate-specific protein), expression vectors comprising such polynucleotides and host cells transformed or transfected with such expression vectors.

          Within other aspects, the present invention provides pharmaceutical compositions

20 comprising a polypeptide or polynucleotide as described above and a physiologically acceptable carrier.

          Within a related aspect of the present invention, vaccines for prophylactic or therapeutic use are provided. Such vaccines comprise a polypeptide or polynucleotide as described above and an immunostimulant.

25   The present invention further provides pharmaceutical compositions that comprise: (a) an antibody or antigen-binding fragment thereof that specifically binds to a prostate-specific protein; and (b) a physiologically acceptable carrier. In certain embodiments, the present invention provides monoclonal antibodies that specifically bind to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 522 and 541-550, together with

30 monoclonal antibodies comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

Within further aspects, the present invention provides pharmaceutical compositions comprising: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) a pharmaceutically acceptable carrier or excipient. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B cells.

Within related aspects, vaccines are provided that comprise: (a) an antigen presenting cell that expresses a polypeptide as described above and (b) an immunostimulant.

The present invention further provides, in other aspects, fusion proteins that comprise at least one polypeptide as described above, as well as polynucleotides encoding such fusion proteins.

Within related aspects, pharmaceutical compositions comprising a fusion protein, or a polynucleotide encoding a fusion protein, in combination with a physiologically acceptable carrier are provided.

Vaccines are further provided, within other aspects, that comprise a fusion protein, or a polynucleotide encoding a fusion protein, in combination with an immunostimulant.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient a pharmaceutical composition or vaccine as recited above.

The present invention further provides, within other aspects, methods for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the protein from the sample.

Within related aspects, methods are provided for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated as described above.

Methods are further provided, within other aspects, for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with one or more of: (i) a polypeptide as described above; (ii) a polynucleotide encoding such a polypeptide; and/or (iii) an antigen presenting cell that expresses such a polypeptide; under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells. Isolated T cell populations comprising T cells prepared as described above are also provided.

Within further aspects, the present invention provides methods for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population as described above.

The present invention further provides methods for inhibiting the development of a cancer in a patient, comprising the steps of: (a) incubating $CD4^+$ and/or $CD8^+$ T cells isolated from a patient with one or more of: (i) a polypeptide comprising at least an immunogenic portion of a prostate-specific protein; (ii) a polynucleotide encoding such a polypeptide; and (iii) an antigen-presenting cell that expressed such a polypeptide; and (b) administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient. Proliferated cells may, but need not, be cloned prior to administration to the patient.

Within further aspects, the present invention provides methods for determining the presence or absence of a cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; and (c) comparing the amount of polypeptide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within preferred embodiments, the binding agent is an antibody, more preferably a monoclonal antibody. The cancer may be prostate cancer.

The present invention also provides, within other aspects, methods for monitoring the progression of a cancer in a patient. Such methods comprise the steps of: (a) contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a polypeptide as recited above; (b) detecting in the sample an amount of polypeptide that binds to the binding agent; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polypeptide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

The present invention further provides, within other aspects, methods for determining the presence or absence of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample a level of a polynucleotide, preferably mRNA, that hybridizes to the oligonucleotide; and (c) comparing the level of polynucleotide that hybridizes to the oligonucleotide with a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient. Within certain

embodiments, the amount of mRNA is detected via polymerase chain reaction using, for example, at least one oligonucleotide primer that hybridizes to a polynucleotide encoding a polypeptide as recited above, or a complement of such a polynucleotide. Within other embodiments, the amount of mRNA is detected using a hybridization technique, employing an oligonucleotide probe that hybridizes to a polynucleotide that encodes a polypeptide as recited above, or a complement of such a polynucleotide.

In related aspects, methods are provided for monitoring the progression of a cancer in a patient, comprising the steps of: (a) contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein; (b) detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and (d) comparing the amount of polynucleotide detected in step (c) with the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

Within further aspects, the present invention provides antibodies, such as monoclonal antibodies, that bind to a polypeptide as described above, as well as diagnostic kits comprising such antibodies. Diagnostic kits comprising one or more oligonucleotide probes or primers as described above are also provided.

These and other aspects of the present invention will become apparent upon reference to the following detailed description and attached drawings. All references disclosed herein are hereby incorporated by reference in their entirety as if each was incorporated individually.

BRIEF DESCRIPTION OF THE DRAWINGS AND SEQUENCE IDENTIFIERS

Figure 1 illustrates the ability of T cells to kill fibroblasts expressing the representative prostate-specific polypeptide P502S, as compared to control fibroblasts. The percentage lysis is shown as a series of effector:target ratios, as indicated.

Figures 2A and 2B illustrate the ability of T cells to recognize cells expressing the representative prostate-specific polypeptide P502S. In each case, the number of γ-interferon spots is shown for different numbers of responders. In Figure 2A, data is presented for fibroblasts pulsed with the P2S-12 peptide, as compared to fibroblasts pulsed with a control E75 peptide. In Figure 2B, data is presented for fibroblasts expressing P502S, as compared to fibroblasts expressing HER-2/neu.

Figure 3 represents a peptide competition binding assay showing that the P1S#10 peptide, derived from P501S, binds HLA-A2. Peptide P1S#10 inhibits HLA-A2 restricted presentation of fluM58 peptide to CTL clone D150M58 in TNF release bioassay. D150M58 CTL is specific for the HLA-A2 binding influenza matrix peptide fluM58.

Figure 4 illustrates the ability of T cell lines generated from P1S#10 immunized mice to specifically lyse P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat A2Kb targets, as compared to EGFP-transduced Jurkat A2Kb. The percent lysis is shown as a series of effector to target ratios, as indicated.

Figure 5 illustrates the ability of a T cell clone to recognize and specifically lyse Jurkat A2Kb cells expressing the representative prostate-specific polypeptide P501S, thereby demonstrating that the P1S#10 peptide may be a naturally processed epitope of the P501S polypeptide.

Figures 6A and 6B are graphs illustrating the specificity of a CD8$^+$ cell line (3A-1) for a representative prostate-specific antigen (P501S). Figure 6A shows the results of a ^{51}Cr release assay. The percent specific lysis is shown as a series of effector:target ratios, as indicated. Figure 6B shows the production of interferon-gamma by 3A-1 cells stimulated with autologous B-LCL transduced with P501S, at varying effector:target rations as indicated.

Figure 7 is a Western blot showing the expression of P501S in baculovirus.

Figure 8 illustrates the results of epitope mapping studies on P501S.

Figure 9 is a schematic representation of the P501S protein showing the location of transmembrane domains and predicted intracellular and extracellular domains.

Figure 10 is a genomic map showing the location of the prostate genes P775P, P704P, B305D, P712P and P774P within the Cat Eye Syndrome region of chromosome 22q11.2

Figure 11 shows the results of an ELISA assay of antibody specificity to P501S peptides.

SEQ ID NO: 1 is the determined cDNA sequence for F1-13

SEQ ID NO: 2 is the determined 3' cDNA sequence for F1-12

SEQ ID NO: 3 is the determined 5' cDNA sequence for F1-12

SEQ ID NO: 4 is the determined 3' cDNA sequence for F1-16

SEQ ID NO: 5 is the determined 3' cDNA sequence for H1-1

SEQ ID NO: 6 is the determined 3' cDNA sequence for H1-9

SEQ ID NO: 7 is the determined 3' cDNA sequence for H1-4

SEQ ID NO: 8 is the determined 3' cDNA sequence for J1-17

SEQ ID NO: 9 is the determined 5' cDNA sequence for J1-17

SEQ ID NO: 10 is the determined 3' cDNA sequence for L1-12

SEQ ID NO: 11 is the determined 5' cDNA sequence for L1-12

5   SEQ ID NO: 12 is the determined 3' cDNA sequence for N1-1862

SEQ ID NO: 13 is the determined 5' cDNA sequence for N1-1862

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SEQ ID NO: 28 is the determined 5' cDNA sequence for L1-14

SEQ ID NO: 29 is the determined 3' cDNA sequence for L1-14

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SEQ ID NO: 35 is the determined 3' cDNA sequence for L1-2

SEQ ID NO: 36 is the determined 3' cDNA sequence for L1-6

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SEQ ID NO: 40 is the determined 3' cDNA sequence for N1-1864

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SEQ ID NO: 43 is the determined cDNA sequence for P9

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SEQ ID NO: 46 is the determined cDNA sequence for P29

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SEQ ID NO: 102 is the determined cDNA sequence for 1D-4288

SEQ ID NO: 103 is the determined cDNA sequence for 1D-4283

SEQ ID NO: 104 is the determined cDNA sequence for 1D-4304

SEQ ID NO: 105 is the determined cDNA sequence for 1D-4296

SEQ ID NO: 106 is the determined cDNA sequence for 1D-4280

SEQ ID NO: 107 is the determined full length cDNA sequence for F1-12 (also referred to as P504S)

5

SEQ ID NO: 108 is the predicted amino acid sequence for F1-12

SEQ ID NO: 109 is the determined full length cDNA sequence for J1-17

SEQ ID NO: 110 is the determined full length cDNA sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 111 is the determined full length cDNA sequence for N1-1862 (also referred to as

10   P503S)

SEQ ID NO: 112 is the predicted amino acid sequence for J1-17

SEQ ID NO: 113 is the predicted amino acid sequence for L1-12 (also referred to as P501S)

SEQ ID NO: 114 is the predicted amino acid sequence for N1-1862 (also referred to as P503S)

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SEQ ID NO: 118 is the determined cDNA sequence for P95

SEQ ID NO: 119 is the determined cDNA sequence for P98

SEQ ID NO: 120 is the determined cDNA sequence for P102

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SEQ ID NO: 123 is the determined cDNA sequence for P114

SEQ ID NO: 124 is the determined cDNA sequence for P115

SEQ ID NO: 125 is the determined cDNA sequence for P116

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SEQ ID NO: 127 is the determined cDNA sequence for P126

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SEQ ID NO: 233 is the determined cDNA sequence for JPTPN25

5   SEQ ID NO: 234 is the determined cDNA sequence for JPTPN30

SEQ ID NO: 235 is the determined cDNA sequence for JPTPN34

SEQ ID NO: 236 is the determined cDNA sequence for PTPN35

SEQ ID NO: 237 is the determined cDNA sequence for JPTPN36

SEQ ID NO: 238 is the determined cDNA sequence for JPTPN38

10   SEQ ID NO: 239 is the determined cDNA sequence for JPTPN39

SEQ ID NO: 240 is the determined cDNA sequence for JPTPN40

SEQ ID NO: 241 is the determined cDNA sequence for JPTPN41

SEQ ID NO: 242 is the determined cDNA sequence for JPTPN42

SEQ ID NO: 243 is the determined cDNA sequence for JPTPN45

15   SEQ ID NO: 244 is the determined cDNA sequence for JPTPN46

SEQ ID NO: 245 is the determined cDNA sequence for JPTPN51

SEQ ID NO: 246 is the determined cDNA sequence for JPTPN56

SEQ ID NO: 247 is the determined cDNA sequence for PTPN64

SEQ ID NO: 248 is the determined cDNA sequence for JPTPN65

20   SEQ ID NO: 249 is the determined cDNA sequence for JPTPN67

SEQ ID NO: 250 is the determined cDNA sequence for JPTPN76

SEQ ID NO: 251 is the determined cDNA sequence for JPTPN84

SEQ ID NO: 252 is the determined cDNA sequence for JPTPN85

SEQ ID NO: 253 is the determined cDNA sequence for JPTPN86

25   SEQ ID NO: 254 is the determined cDNA sequence for JPTPN87

SEQ ID NO: 255 is the determined cDNA sequence for JPTPN88

SEQ ID NO: 256 is the determined cDNA sequence for JP1F1

SEQ ID NO: 257 is the determined cDNA sequence for JP1F2

SEQ ID NO: 258 is the determined cDNA sequence for JP1C2

30   SEQ ID NO: 259 is the determined cDNA sequence for JP1B1

SEQ ID NO: 260 is the determined cDNA sequence for JP1B2

SEQ ID NO: 261 is the determined cDNA sequence for JP1D3

SEQ ID NO: 262 is the determined cDNA sequence for JP1A4

SEQ ID NO: 263 is the determined cDNA sequence for JP1F5

SEQ ID NO: 264 is the determined cDNA sequence for JP1E6

SEQ ID NO: 265 is the determined cDNA sequence for JP1D6

5   SEQ ID NO: 266 is the determined cDNA sequence for JP1B5

SEQ ID NO: 267 is the determined cDNA sequence for JP1A6

SEQ ID NO: 268 is the determined cDNA sequence for JP1E8

SEQ ID NO: 269 is the determined cDNA sequence for JP1D7

SEQ ID NO: 270 is the determined cDNA sequence for JP1D9

10   SEQ ID NO: 271 is the determined cDNA sequence for JP1C10

SEQ ID NO: 272 is the determined cDNA sequence for JP1A9

SEQ ID NO: 273 is the determined cDNA sequence for JP1F12

SEQ ID NO: 274 is the determined cDNA sequence for JP1E12

SEQ ID NO: 275 is the determined cDNA sequence for JP1D11

15   SEQ ID NO: 276 is the determined cDNA sequence for JP1C11

SEQ ID NO: 277 is the determined cDNA sequence for JP1C12

SEQ ID NO: 278 is the determined cDNA sequence for JP1B12

SEQ ID NO: 279 is the determined cDNA sequence for JP1A12

SEQ ID NO: 280 is the determined cDNA sequence for JP8G2

20   SEQ ID NO: 281 is the determined cDNA sequence for JP8H1

SEQ ID NO: 282 is the determined cDNA sequence for JP8H2

SEQ ID NO: 283 is the determined cDNA sequence for JP8A3

SEQ ID NO: 284 is the determined cDNA sequence for JP8A4

SEQ ID NO: 285 is the determined cDNA sequence for JP8C3

25   SEQ ID NO: 286 is the determined cDNA sequence for JP8G4

SEQ ID NO: 287 is the determined cDNA sequence for JP8B6

SEQ ID NO: 288 is the determined cDNA sequence for JP8D6

SEQ ID NO: 289 is the determined cDNA sequence for JP8F5

SEQ ID NO: 290 is the determined cDNA sequence for JP8A8

30   SEQ ID NO: 291 is the determined cDNA sequence for JP8C7

SEQ ID NO: 292 is the determined cDNA sequence for JP8D7

SEQ ID NO: 293 is the determined cDNA sequence for P8D8

SEQ ID NO: 294 is the determined cDNA sequence for JP8E7

SEQ ID NO: 295 is the determined cDNA sequence for JP8F8

SEQ ID NO: 296 is the determined cDNA sequence for JP8G8

SEQ ID NO: 297 is the determined cDNA sequence for JP8B10

SEQ ID NO: 298 is the determined cDNA sequence for JP8C10

SEQ ID NO: 299 is the determined cDNA sequence for JP8E9

SEQ ID NO: 300 is the determined cDNA sequence for JP8E10

SEQ ID NO: 301 is the determined cDNA sequence for JP8F9

SEQ ID NO: 302 is the determined cDNA sequence for JP8H9

SEQ ID NO: 303 is the determined cDNA sequence for JP8C12

SEQ ID NO: 304 is the determined cDNA sequence for JP8E11

SEQ ID NO: 305 is the determined cDNA sequence for JP8E12

SEQ ID NO: 306 is the amino acid sequence for the peptide PS2#12

SEQ ID NO: 307 is the determined cDNA sequence for P711P

SEQ ID NO: 308 is the determined cDNA sequence for P712P

SEQ ID NO: 309 is the determined cDNA sequence for CLONE23

SEQ ID NO: 310 is the determined cDNA sequence for P774P

SEQ ID NO: 311 is the determined cDNA sequence for P775P

SEQ ID NO: 312 is the determined cDNA sequence for P715P

SEQ ID NO: 313 is the determined cDNA sequence for P710P

SEQ ID NO: 314 is the determined cDNA sequence for P767P

SEQ ID NO: 315 is the determined cDNA sequence for P768P

SEQ ID NO: 316-325 are the determined cDNA sequences of previously isolated genes

SEQ ID NO: 326 is the determined cDNA sequence for P703PDE5

SEQ ID NO: 327 is the predicted amino acid sequence for P703PDE5

SEQ ID NO: 328 is the determined cDNA sequence for P703P6.26

SEQ ID NO: 329 is the predicted amino acid sequence for P703P6.26

SEQ ID NO: 330 is the determined cDNA sequence for P703PX-23

SEQ ID NO: 331 is the predicted amino acid sequence for P703PX-23

SEQ ID NO: 332 is the determined full length cDNA sequence for P509S

SEQ ID NO: 333 is the determined extended cDNA sequence for P707P (also referred to as 11-C9)

SEQ ID NO: 334 is the determined cDNA sequence for P714P

SEQ ID NO: 335 is the determined cDNA sequence for P705P (also referred to as 9-F3)

SEQ ID NO: 336 is the predicted amino acid sequence for P705P

SEQ ID NO: 337 is the amino acid sequence of the peptide P1S#10

SEQ ID NO: 338 is the amino acid sequence of the peptide p5

SEQ ID NO: 339 is the predicted amino acid sequence of P509S

SEQ ID NO: 340 is the determined cDNA sequence for P778P

SEQ ID NO: 341 is the determined cDNA sequence for P786P

SEQ ID NO: 342 is the determined cDNA sequence for P789P

SEQ ID NO: 343 is the determined cDNA sequence for a clone showing homology to Homo

sapiens MM46 mRNA

SEQ ID NO: 344 is the determined cDNA sequence for a clone showing homology to Homo

sapiens TNF-alpha stimulated ABC protein (ABC50) mRNA

SEQ ID NO: 345 is the determined cDNA sequence for a clone showing homology to Homo

sapiens mRNA for E-cadherin

SEQ ID NO: 346 is the determined cDNA sequence for a clone showing homology to Human

nuclear-encoded mitochondrial serine hydroxymethyltransferase (SHMT)

SEQ ID NO: 347 is the determined cDNA sequence for a clone showing homology to Homo

sapiens natural resistance-associated macrophage protein2 (NRAMP2)

SEQ ID NO: 348 is the determined cDNA sequence for a clone showing homology to Homo

sapiens phosphoglucomutase-related protein (PGMRP)

SEQ ID NO: 349 is the determined cDNA sequence for a clone showing homology to Human

mRNA for proteosome subunit p40

SEQ ID NO: 350 is the determined cDNA sequence for P777P

SEQ ID NO: 351 is the determined cDNA sequence for P779P

SEQ ID NO: 352 is the determined cDNA sequence for P790P

SEQ ID NO: 353 is the determined cDNA sequence for P784P

SEQ ID NO: 354 is the determined cDNA sequence for P776P

SEQ ID NO: 355 is the determined cDNA sequence for P780P

SEQ ID NO: 356 is the determined cDNA sequence for P544S

SEQ ID NO: 357 is the determined cDNA sequence for P745S

SEQ ID NO: 358 is the determined cDNA sequence for P782P

SEQ ID NO: 359 is the determined cDNA sequence for P783P

SEQ ID NO: 360 is the determined cDNA sequence for unknown 17984

SEQ ID NO: 361 is the determined cDNA sequence for P787P

SEQ ID NO: 362 is the determined cDNA sequence for P788P

SEQ ID NO: 363 is the determined cDNA sequence for unknown 17994

5 SEQ ID NO: 364 is the determined cDNA sequence for P781P

SEQ ID NO: 365 is the determined cDNA sequence for P785P

SEQ ID NO: 366-375 are the determined cDNA sequences for splice variants of B305D.

SEQ ID NO: 376 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 366.

10 SEQ ID NO: 377 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 372.

SEQ ID NO: 378 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 373.

SEQ ID NO: 379 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15 374.

SEQ ID NO: 380 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 375.

SEQ ID NO: 381 is the determined cDNA sequence for B716P.

SEQ ID NO: 382 is the determined full-length cDNA sequence for P711P.

20 SEQ ID NO: 383 is the predicted amino acid sequence for P711P.

SEQ ID NO: 384 is the cDNA sequence for P1000C.

SEQ ID NO: 385 is the cDNA sequence for CGI-82.

SEQ ID NO:386 is the cDNA sequence for 23320.

SEQ ID NO:387 is the cDNA sequence for CGI-69.

25 SEQ ID NO:388 is the cDNA sequence for L-iditol-2-dehydrogenase.

SEQ ID NO:389 is the cDNA sequence for 23379.

SEQ ID NO:390 is the cDNA sequence for 23381.

SEQ ID NO:391 is the cDNA sequence for KIAA0122.

SEQ ID NO:392 is the cDNA sequence for 23399.

30 SEQ ID NO:393 is the cDNA sequence for a previously identified gene.

SEQ ID NO:394 is the cDNA sequence for HCLBP.

SEQ ID NO:395 is the cDNA sequence for transglutaminase.

SEQ ID NO:396 is the cDNA sequence for a previously identified gene.

SEQ ID NO:397 is the cDNA sequence for PAP.

SEQ ID NO:398 is the cDNA sequence for Ets transcription factor PDEF.

SEQ ID NO:399 is the cDNA sequence for hTGR.

5   SEQ ID NO:400 is the cDNA sequence for KIAA0295.

SEQ ID NO:401 is the cDNA sequence for 22545.

SEQ ID NO:402 is the cDNA sequence for 22547.

SEQ ID NO:403 is the cDNA sequence for 22548.

SEQ ID NO:404 is the cDNA sequence for 22550.

10   SEQ ID NO:405 is the cDNA sequence for 22551.

SEQ ID NO:406 is the cDNA sequence for 22552.

SEQ ID NO:407 is the cDNA sequence for 22553.

SEQ ID NO:408 is the cDNA sequence for 22558.

SEQ ID NO:409 is the cDNA sequence for 22562.

15   SEQ ID NO:410 is the cDNA sequence for 22565.

SEQ ID NO:411 is the cDNA sequence for 22567.

SEQ ID NO:412 is the cDNA sequence for 22568.

SEQ ID NO:413 is the cDNA sequence for 22570.

SEQ ID NO:414 is the cDNA sequence for 22571.

20   SEQ ID NO:415 is the cDNA sequence for 22572.

SEQ ID NO:416 is the cDNA sequence for 22573.

SEQ ID NO:417 is the cDNA sequence for 22573.

SEQ ID NO:418 is the cDNA sequence for 22575.

SEQ ID NO:419 is the cDNA sequence for 22580.

25   SEQ ID NO:420 is the cDNA sequence for 22581.

SEQ ID NO:421 is the cDNA sequence for 22582.

SEQ ID NO:422 is the cDNA sequence for 22583.

SEQ ID NO:423 is the cDNA sequence for 22584.

SEQ ID NO:424 is the cDNA sequence for 22585.

30   SEQ ID NO:425 is the cDNA sequence for 22586.

SEQ ID NO:426 is the cDNA sequence for 22587.

SEQ ID NO:427 is the cDNA sequence for 22588.

SEQ ID NO:428 is the cDNA sequence for 22589.

SEQ ID NO:429 is the cDNA sequence for 22590.

SEQ ID NO:430 is the cDNA sequence for 22591.

SEQ ID NO:431 is the cDNA sequence for 22592.

5   SEQ ID NO:432 is the cDNA sequence for 22593.

SEQ ID NO:433 is the cDNA sequence for 22594.

SEQ ID NO:434 is the cDNA sequence for 22595.

SEQ ID NO:435 is the cDNA sequence for 22596.

SEQ ID NO:436 is the cDNA sequence for 22847.

10   SEQ ID NO:437 is the cDNA sequence for 22848.

SEQ ID NO:438 is the cDNA sequence for 22849.

SEQ ID NO:439 is the cDNA sequence for 22851.

SEQ ID NO:440 is the cDNA sequence for 22852.

SEQ ID NO:441 is the cDNA sequence for 22853.

15   SEQ ID NO:442 is the cDNA sequence for 22854.

SEQ ID NO:443 is the cDNA sequence for 22855.

SEQ ID NO:444 is the cDNA sequence for 22856.

SEQ ID NO:445 is the cDNA sequence for 22857.

SEQ ID NO:446 is the cDNA sequence for 23601.

20   SEQ ID NO:447 is the cDNA sequence for 23602.

SEQ ID NO:448 is the cDNA sequence for 23605.

SEQ ID NO:449 is the cDNA sequence for 23606.

SEQ ID NO:450 is the cDNA sequence for 23612.

SEQ ID NO:451 is the cDNA sequence for 23614.

25   SEQ ID NO:452 is the cDNA sequence for 23618.

SEQ ID NO:453 is the cDNA sequence for 23622.

SEQ ID NO:454 is the cDNA sequence for folate hydrolase.

SEQ ID NO:455 is the cDNA sequence for LIM protein.

SEQ ID NO:456 is the cDNA sequence for a known gene.

30   SEQ ID NO:457 is the cDNA sequence for a known gene.

SEQ ID NO:458 is the cDNA sequence for a previously identified gene.

SEQ ID NO:459 is the cDNA sequence for 23045.

SEQ ID NO:460 is the cDNA sequence for 23032.

SEQ ID NO:461 is the cDNA sequence for 23054.

SEQ ID NO:462-467 are cDNA sequences for known genes.

SEQ ID NO:468-471 are cDNA sequences for P710P.

5   SEQ ID NO:472 is a cDNA sequence for P1001C.

SEQ ID NO: 473 is the determined cDNA sequence for a first splice variant of P775P (referred to as 27505).

SEQ ID NO: 474 is the determined cDNA sequence for a second splice variant of P775P (referred to as 19947).

10   SEQ ID NO: 475 is the determined cDNA sequence for a third splice variant of P775P (referred to as 19941).

SEQ ID NO: 476 is the determined cDNA sequence for a fourth splice variant of P775P (referred to as 19937).

SEQ ID NO: 477 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 15   474.

SEQ ID NO: 478 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 474.

SEQ ID NO: 479 is the predicted amino acid sequence encoded by the sequence of SEQ ID NO: 475.

20   SEQ ID NO: 480 is a first predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 481 is a second predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 482 is a third predicted amino acid sequence encoded by the sequence of SEQ ID NO: 25   473.

SEQ ID NO: 483 is a fourth predicted amino acid sequence encoded by the sequence of SEQ ID NO: 473.

SEQ ID NO: 484 is the first 30 amino acids of the *M. tuberculosis* antigen Ra12.

SEQ ID NO: 485 is the PCR primer AW025.

30   SEQ ID NO: 486 is the PCR primer AW003.

SEQ ID NO: 487 is the PCR primer AW027.

SEQ ID NO: 488 is the PCR primer AW026.

SEQ ID NO: 489-501 are peptides employed in epitope mapping studies.

SEQ ID NO: 502 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody 20D4.

SEQ ID NO: 503 is the determined cDNA sequence of the complementarity determining region for the anti-P503S monoclonal antibody JA1.

SEQ ID NO: 504 & 505 are peptides employed in epitope mapping studies.

SEQ ID NO: 506 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 8H2.

SEQ ID NO: 507 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 7H8.

SEQ ID NO: 508 is the determined cDNA sequence of the complementarity determining region for the anti-P703P monoclonal antibody 2D4.

SEQ ID NO: 509-522 are peptides employed in epitope mapping studies.

SEQ ID NO: 523 is a mature form of P703P used to raise antibodies against P703P.SEQ ID NO: 524 is the putative full-length cDNA sequence of P703P.

SEQ ID NO: 525 is the predicted amino acid sequence encoded by SEQ ID NO: 524.

SEQ ID NO: 526 is the full-length cDNA sequence for P790P.

SEQ ID NO: 527 is the predicted amino acid sequence for P790P.

SEQ ID NO: 528 & 529 are PCR primers.

SEQ ID NO: 530 is the cDNA sequence of a splice variant of SEQ ID NO: 366.

SEQ ID NO: 531 is the cDNA sequence of the open reading frame of SEQ ID NO: 530.

SEQ ID NO: 532 is the predicted amino acid encoded by the sequence of SEQ ID NO: 531.

SEQ ID NO: 533 is the DNA sequence of a putative ORF of P775P.

SEQ ID NO: 534 is the predicted amino acid sequence encoded by SEQ ID NO: 533.

SEQ ID NO: 535 is a first full-length cDNA sequence for P510S.

SEQ ID NO: 536 is a second full-length cDNA sequence for P510S.

SEQ ID NO: 537 is the predicted amino acid sequence encoded by SEQ ID NO: 535.

SEQ ID NO: 538 is the predicted amino acid sequence encoded by SEQ ID NO: 536.

SEQ ID NO: 539 is the peptide P501S-370.

SEQ ID NO: 540 is the peptide P501S-376.

SEQ ID NO: 541-550 are epitopes of P501S.

SEQ ID NO: 551 corresponds to amino acids 543-553 of P501S.

DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy and diagnosis of cancer, such as prostate cancer. The compositions described herein may include prostate-specific polypeptides, polynucleotides encoding such polypeptides, binding agents such as antibodies, antigen presenting cells (APCs) and/or immune system cells (e.g., T cells). Polypeptides of the present invention generally comprise at least a portion (such as an immunogenic portion) of a prostate-specific protein or a variant thereof. A "prostate-specific protein" is a protein that is expressed in normal prostate and/or prostate tumor cells at a level that is at least two fold, and preferably at least five fold, greater than the level of expression in a non-prostate normal tissue, as determined using a representative assay provided herein. Certain prostate-specific proteins are proteins that react detectably (within an immunoassay, such as an ELISA or Western blot) with antisera of a patient afflicted with prostate cancer. Polynucleotides of the subject invention generally comprise a DNA or RNA sequence that encodes all or a portion of such a polypeptide, or that is complementary to such a sequence. Antibodies are generally immune system proteins, or antigen-binding fragments thereof, that are capable of binding to a polypeptide as described above. Antigen presenting cells include dendritic cells, macrophages, monocytes, fibroblasts and B-cells that express a polypeptide as described above. T cells that may be employed within such compositions are generally T cells that are specific for a polypeptide as described above.

The present invention is based on the discovery of human prostate-specific proteins. Sequences of polynucleotides encoding certain prostate-specific proteins, or portions thereof, are provided in SEQ ID NOs:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Sequences of polypeptides comprising at least a portion of a prostate-specific protein are provided in SEQ ID NOs:112-114, 172, 176, 178, 327, 329, 331, 336, 339, 376-380, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

PROSTATE-SPECIFIC PROTEIN POLYNUCLEOTIDES

Any polynucleotide that encodes a prostate-specific protein or a portion or other variant thereof as described herein is encompassed by the present invention. Preferred

polynucleotides comprise at least 15 consecutive nucleotides, preferably at least 30 consecutive nucleotides and more preferably at least 45 consecutive nucleotides, that encode a portion of a prostate-specific protein. More preferably, a polynucleotide encodes an immunogenic portion of a prostate-specific protein. Polynucleotides complementary to any such sequences are also encompassed by the present invention. Polynucleotides may be single-stranded (coding or antisense) or double-stranded, and may be DNA (genomic, cDNA or synthetic) or RNA molecules. RNA molecules include HnRNA molecules, which contain introns and correspond to a DNA molecule in a one-to-one manner, and mRNA molecules, which do not contain introns. Additional coding or non-coding sequences may, but need not, be present within a polynucleotide of the present invention, and a polynucleotide may, but need not, be linked to other molecules and/or support materials.

Polynucleotides may comprise a native sequence (i.e., an endogenous sequence that encodes a prostate-specific protein or a portion thereof) or may comprise a variant of such a sequence. Polynucleotide variants may contain one or more substitutions, additions, deletions and/or insertions such that the immunogenicity of the encoded polypeptide is not diminished, relative to a native protein. The effect on the immunogenicity of the encoded polypeptide may generally be assessed as described herein. Variants preferably exhibit at least about 70% identity, more preferably at least about 80% identity and most preferably at least about 90% identity to a polynucleotide sequence that encodes a native prostate-specific protein or a portion thereof. The term "variants" also encompasses homologous genes of xenogenic origin.

Two polynucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acids in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins – Matrices

for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenes pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) *CABIOS 5*:151-

5   153; Myers, E.W. and Muller W. (1988) *CABIOS 4*:11-17; Robinson, E.D. (1971) *Comb. Theor 11*:105; Santou, N. Nes, M. (1987) *Mol. Biol. Evol. 4*:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy – the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) *Proc. Natl. Acad., Sci. USA 80*:726-730.

Preferably, the "percentage of sequence identity" is determined by comparing two
10   optimally aligned sequences over a window of comparison of at least 20 positions, wherein the portion of the polynucleotide or polypeptide sequence in the comparison window may comprise additions or deletions (*i.e.,* gaps) of 20 percent or less, usually 5 to 15 percent, or 10 to 12 percent, as compared to the reference sequences (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage is calculated by determining the number of
15   positions at which the identical nucleic acid bases or amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the reference sequence (*i.e.,* the window size) and multiplying the results by 100 to yield the percentage of sequence identity.

Variants may also, or alternatively, be substantially homologous to a native gene, or
20   a portion or complement thereof. Such polynucleotide variants are capable of hybridizing under moderately stringent conditions to a naturally occurring DNA sequence encoding a native prostate-specific protein (or a complementary sequence). Suitable moderately stringent conditions include prewashing in a solution of 5 X SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5 X SSC, overnight; followed by washing twice at 65°C for 20 minutes with each of 2X,
25   0.5X and 0.2X SSC containing 0.1% SDS.

It will be appreciated by those of ordinary skill in the art that, as a result of the degeneracy of the genetic code, there are many nucleotide sequences that encode a polypeptide as described herein. Some of these polynucleotides bear minimal homology to the nucleotide sequence of any native gene. Nonetheless, polynucleotides that vary due to differences in codon
30   usage are specifically contemplated by the present invention. Further, alleles of the genes comprising the polynucleotide sequences provided herein are within the scope of the present invention. Alleles are endogenous genes that are altered as a result of one or more mutations, such

as deletions, additions and/or substitutions of nucleotides. The resulting mRNA and protein may, but need not, have an altered structure or function. Alleles may be identified using standard techniques (such as hybridization, amplification and/or database sequence comparison).

Polynucleotides may be prepared using any of a variety of techniques. For example, a polynucleotide may be identified, as described in more detail below, by screening a microarray of cDNAs for tumor-associated expression (*i.e.*, expression that is at least five fold greater in a prostate-specific than in normal tissue, as determined using a representative assay provided herein). Such screens may be performed using a Synteni microarray (Palo Alto, CA) according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA 93*:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA 94*:2150-2155, 1997). Alternatively, polypeptides may be amplified from cDNA prepared from cells expressing the proteins described herein, such as prostate-specific cells. Such polynucleotides may be amplified via polymerase chain reaction (PCR). For this approach, sequence-specific primers may be designed based on the sequences provided herein, and may be purchased or synthesized.

An amplified portion may be used to isolate a full length gene from a suitable library (*e.g.*, a prostate-specific cDNA library) using well known techniques. Within such techniques, a library (cDNA or genomic) is screened using one or more polynucleotide probes or primers suitable for amplification. Preferably, a library is size-selected to include larger molecules. Random primed libraries may also be preferred for identifying 5' and upstream regions of genes. Genomic libraries are preferred for obtaining introns and extending 5' sequences.

For hybridization techniques, a partial sequence may be labeled (*e.g.*, by nick-translation or end-labeling with ^{32}P) using well known techniques. A bacterial or bacteriophage library is then screened by hybridizing filters containing denatured bacterial colonies (or lawns containing phage plaques) with the labeled probe (*see* Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY, 1989). Hybridizing colonies or plaques are selected and expanded, and the DNA is isolated for further analysis. cDNA clones may be analyzed to determine the amount of additional sequence by, for example, PCR using a primer from the partial sequence and a primer from the vector. Restriction maps and partial sequences may be generated to identify one or more overlapping clones. The complete sequence may then be determined using standard techniques, which may involve generating a series of deletion clones. The resulting overlapping sequences are then assembled into

a single contiguous sequence. A full length cDNA molecule can be generated by ligating suitable fragments, using well known techniques.

Alternatively, there are numerous amplification techniques for obtaining a full length coding sequence from a partial cDNA sequence. Within such techniques, amplification is generally 5 performed via PCR. Any of a variety of commercially available kits may be used to perform the amplification step. Primers may be designed using, for example, software well known in the art. Primers are preferably 22-30 nucleotides in length, have a GC content of at least 50% and anneal to the target sequence at temperatures of about 68°C to 72°C. The amplified region may be sequenced as described above, and overlapping sequences assembled into a contiguous sequence.

10 One such amplification technique is inverse PCR (*see* Triglia et al., *Nucl. Acids Res. 16*:8186, 1988), which uses restriction enzymes to generate a fragment in the known region of the gene. The fragment is then circularized by intramolecular ligation and used as a template for PCR with divergent primers derived from the known region. Within an alternative approach, sequences adjacent to a partial sequence may be retrieved by amplification with a primer to a linker sequence 15 and a primer specific to a known region. The amplified sequences are typically subjected to a second round of amplification with the same linker primer and a second primer specific to the known region. A variation on this procedure, which employs two primers that initiate extension in opposite directions from the known sequence, is described in WO 96/38591. Another such technique is known as "rapid amplification of cDNA ends" or RACE. This technique involves the 20 use of an internal primer and an external primer, which hybridizes to a polyA region or vector sequence, to identify sequences that are 5' and 3' of a known sequence. Additional techniques include capture PCR (Lagerstrom et al., *PCR Methods Applic. 1*:111-19, 1991) and walking PCR (Parker et al., *Nucl. Acids. Res. 19*:3055-60, 1991). Other methods employing amplification may also be employed to obtain a full length cDNA sequence.

25 In certain instances, it is possible to obtain a full length cDNA sequence by analysis of sequences provided in an expressed sequence tag (EST) database, such as that available from GenBank. Searches for overlapping ESTs may generally be performed using well known programs (*e.g.*, NCBI BLAST searches), and such ESTs may be used to generate a contiguous full length sequence. Full length DNA sequences may also be obtained by analysis of genomic fragments.

30 Certain nucleic acid sequences of cDNA molecules encoding at least a portion of a prostate-specific protein are provided in SEQ ID NO:1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536.

Isolation of these polynucleotides is described below. Each of these prostate-specific proteins was overexpressed in prostate tumor tissue.

Polynucleotide variants may generally be prepared by any method known in the art, including chemical synthesis by, for example, solid phase phosphoramidite chemical synthesis.
5 Modifications in a polynucleotide sequence may also be introduced using standard mutagenesis techniques, such as oligonucleotide-directed site-specific mutagenesis (see Adelman et al., *DNA* 2:183, 1983). Alternatively, RNA molecules may be generated by *in vitro* or *in vivo* transcription of DNA sequences encoding a prostate-specific protein, or portion thereof, provided that the DNA is incorporated into a vector with a suitable RNA polymerase promoter (such as T7 or SP6). Certain
10 portions may be used to prepare an encoded polypeptide, as described herein. In addition, or alternatively, a portion may be administered to a patient such that the encoded polypeptide is generated *in vivo* (e.g., by transfecting antigen-presenting cells, such as dendritic cells, with a cDNA construct encoding a prostate-specific polypeptide, and administering the transfected cells to the patient).

15   A portion of a sequence complementary to a coding sequence (i.e., an antisense polynucleotide) may also be used as a probe or to modulate gene expression. cDNA constructs that can be transcribed into antisense RNA may also be introduced into cells of tissues to facilitate the production of antisense RNA. An antisense polynucleotide may be used, as described herein, to inhibit expression of a protein. Antisense technology can be used to control gene expression
20 through triple-helix formation, which compromises the ability of the double helix to open sufficiently for the binding of polymerases, transcription factors or regulatory molecules (see Gee et al., *In* Huber and Carr, *Molecular and Immunologic Approaches*, Futura Publishing Co. (Mt. Kisco, NY; 1994)). Alternatively, an antisense molecule may be designed to hybridize with a control region of a gene (e.g., promoter, enhancer or transcription initiation site), and block transcription of
25 the gene; or to block translation by inhibiting binding of a transcript to ribosomes.

A portion of a coding sequence, or of a complementary sequence, may also be designed as a probe or primer to detect gene expression. Probes may be labeled with a variety of reporter groups, such as radionuclides and enzymes, and are preferably at least 10 nucleotides in length, more preferably at least 20 nucleotides in length and still more preferably at least 30
30 nucleotides in length. Primers, as noted above, are preferably 22-30 nucleotides in length.

Any polynucleotide may be further modified to increase stability *in vivo*. Possible modifications include, but are not limited to, the addition of flanking sequences at the 5' and/or 3'

ends; the use of phosphorothioate or 2' O-methyl rather than phosphodiesterase linkages in the backbone; and/or the inclusion of nontraditional bases such as inosine, queosine and wybutosine, as well as acetyl- methyl-, thio- and other modified forms of adenine, cytidine, guanine, thymine and uridine.

5   Nucleotide sequences as described herein may be joined to a variety of other nucleotide sequences using established recombinant DNA techniques.   For example, a polynucleotide may be cloned into any of a variety of cloning vectors, including plasmids, phagemids, lambda phage derivatives and cosmids. Vectors of particular interest include expression vectors, replication vectors, probe generation vectors and sequencing vectors. In general, a vector
10   will contain an origin of replication functional in at least one organism, convenient restriction endonuclease sites and one or more selectable markers. Other elements will depend upon the desired use, and will be apparent to those of ordinary skill in the art.

          Within certain embodiments, polynucleotides may be formulated so as to permit entry into a cell of a mammal, and expression therein. Such formulations are particularly useful for
15   therapeutic purposes, as described below. Those of ordinary skill in the art will appreciate that there are many ways to achieve expression of a polynucleotide in a target cell, and any suitable method may be employed. For example, a polynucleotide may be incorporated into a viral vector such as, but not limited to, adenovirus, adeno-associated virus, retrovirus, or vaccinia or other pox virus (e.g., avian pox virus). The polynucleotides may also be administered as naked plasmid vectors.
20   Techniques for incorporating DNA into such vectors are well known to those of ordinary skill in the art. A retroviral vector may additionally transfer or incorporate a gene for a selectable marker (to aid in the identification or selection of transduced cells) and/or a targeting moiety, such as a gene that encodes a ligand for a receptor on a specific target cell, to render the vector target specific. Targeting may also be accomplished using an antibody, by methods known to those of ordinary
25   skill in the art.

          Other formulations for therapeutic purposes include colloidal dispersion systems, such as macromolecule complexes, nanocapsules, microspheres, beads, and lipid-based systems including oil-in-water emulsions, micelles, mixed micelles, and liposomes. A preferred colloidal system for use as a delivery vehicle in vitro and in vivo is a liposome (i.e., an artificial membrane
30   vesicle). The preparation and use of such systems is well known in the art.

PROSTATE-SPECIFIC POLYPEPTIDES

Within the context of the present invention, polypeptides may comprise at least an immunogenic portion of a prostate-specific protein or a variant thereof, as described herein. As noted above, a "prostate-specific protein" is a protein that is expressed by normal prostate and/or

5 prostate tumor cells. Proteins that are prostate-specific proteins also react detectably within an immunoassay (such as an ELISA) with antisera from a patient with prostate cancer. Polypeptides as described herein may be of any length. Additional sequences derived from the native protein and/or heterologous sequences may be present, and such sequences may (but need not) possess further immunogenic or antigenic properties.

10 An "immunogenic portion," as used herein is a portion of a protein that is recognized (i.e., specifically bound) by a B-cell and/or T-cell surface antigen receptor. Such immunogenic portions generally comprise at least 5 amino acid residues, more preferably at least 10, and still more preferably at least 20 amino acid residues of a prostate-specific protein or a variant thereof. Certain preferred immunogenic portions include peptides in which an N-terminal leader sequence

15 and/or transmembrane domain have been deleted. Other preferred immunogenic portions may contain a small N- and/or C-terminal deletion (e.g., 1-30 amino acids, preferably 5-15 amino acids), relative to the mature protein.

Immunogenic portions may generally be identified using well known techniques, such as those summarized in Paul, *Fundamental Immunology*, 3rd ed., 243-247 (Raven Press, 1993)

20 and references cited therein. Such techniques include screening polypeptides for the ability to react with antigen-specific antibodies, antisera and/or T-cell lines or clones. As used herein, antisera and antibodies are "antigen-specific" if they specifically bind to an antigen (i.e., they react with the protein in an ELISA or other immunoassay, and do not react detectably with unrelated proteins). Such antisera and antibodies may be prepared as described herein, and using well known

25 techniques. An immunogenic portion of a native prostate-specific protein is a portion that reacts with such antisera and/or T-cells at a level that is not substantially less than the reactivity of the full length polypeptide (e.g., in an ELISA and/or T-cell reactivity assay). Such immunogenic portions may react within such assays at a level that is similar to or greater than the reactivity of the full length polypeptide. Such screens may generally be performed using methods well known to those

30 of ordinary skill in the art, such as those described in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, 1988. For example, a polypeptide may be immobilized on a solid support and contacted with patient sera to allow binding of antibodies within the sera to the

immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, ^{125}I-labeled Protein A.

As noted above, a composition may comprise a variant of a native prostate-specific protein. A polypeptide "variant," as used herein, is a polypeptide that differs from a native prostate-
5   specific protein in one or more substitutions, deletions, additions and/or insertions, such that the immunogenicity of the polypeptide is not substantially diminished. In other words, the ability of a variant to react with antigen-specific antisera may be enhanced or unchanged, relative to the native protein, or may be diminished by less than 50%, and preferably less than 20%, relative to the native protein. Such variants may generally be identified by modifying one of the above polypeptide
10   sequences and evaluating the reactivity of the modified polypeptide with antigen-specific antibodies or antisera as described herein. Preferred variants include those in which one or more portions, such as an N-terminal leader sequence or transmembrane domain, have been removed. Other preferred variants include variants in which a small portion (e.g., 1-30 amino acids, preferably 5-15 amino acids) has been removed from the N- and/or C-terminal of the mature protein. Polypeptide variants
15   preferably exhibit at least about 70%, more preferably at least about 90% and most preferably at least about 95% identity (determined as described above) to the identified polypeptides.

Preferably, a variant contains conservative substitutions. A "conservative substitution" is one in which an amino acid is substituted for another amino acid that has similar properties, such that one skilled in the art of peptide chemistry would expect the secondary structure
20   and hydropathic nature of the polypeptide to be substantially unchanged. Amino acid substitutions may generally be made on the basis of similarity in polarity, charge, solubility, hydrophobicity, hydrophilicity and/or the amphipathic nature of the residues. For example, negatively charged amino acids include aspartic acid and glutamic acid; positively charged amino acids include lysine and arginine; and amino acids with uncharged polar head groups having similar hydrophilicity
25   values include leucine, isoleucine and valine; glycine and alanine; asparagine and glutamine; and serine, threonine, phenylalanine and tyrosine. Other groups of amino acids that may represent conservative changes include: (1) ala, pro, gly, glu, asp, gln, asn, ser, thr; (2) cys, ser, tyr, thr; (3) val, ile, leu, met, ala, phe; (4) lys, arg, his; and (5) phe, tyr, trp, his. A variant may also, or alternatively, contain nonconservative changes. In a preferred embodiment, variant polypeptides
30   differ from a native sequence by substitution, deletion or addition of five amino acids or fewer. Variants may also (or alternatively) be modified by, for example, the deletion or addition of amino

acids that have minimal influence on the immunogenicity, secondary structure and hydropathic nature of the polypeptide.

As noted above, polypeptides may comprise a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the
5 protein. The polypeptide may also be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (*e.g.*, poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.

Polypeptides may be prepared using any of a variety of well known techniques.
10 Recombinant polypeptides encoded by DNA sequences as described above may be readily prepared from the DNA sequences using any of a variety of expression vectors known to those of ordinary skill in the art. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a DNA molecule that encodes a recombinant polypeptide. Suitable host cells include prokaryotes, yeast, higher eukaryotic and plant cells.
15 Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line such as COS or CHO. Supernatants from suitable host/vector systems which secrete recombinant protein or polypeptide into culture media may be first concentrated using a commercially available filter. Following concentration, the concentrate may be applied to a suitable purification matrix such as an affinity matrix or an ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed
20 to further purify a recombinant polypeptide.

Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may also be generated by synthetic means, using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as the Merrifield solid-phase
25 synthesis method, where amino acids are sequentially added to a growing amino acid chain. *See* Merrifield, *J. Am. Chem. Soc.* 85:2149-2146, 1963. Equipment for automated synthesis of polypeptides is commercially available from suppliers such as Perkin Elmer/Applied BioSystems Division (Foster City, CA), and may be operated according to the manufacturer's instructions.

Within certain specific embodiments, a polypeptide may be a fusion protein that
30 comprises multiple polypeptides as described herein, or that comprises at least one polypeptide as described herein and an unrelated sequence, such as a known prostate-specific protein. A fusion partner may, for example, assist in providing T helper epitopes (an immunological fusion partner),

preferably T helper epitopes recognized by humans, or may assist in expressing the protein (an expression enhancer) at higher yields than the native recombinant protein. Certain preferred fusion partners are both immunological and expression enhancing fusion partners. Other fusion partners may be selected so as to increase the solubility of the protein or to enable the protein to be targeted

5   to desired intracellular compartments. Still further fusion partners include affinity tags, which facilitate purification of the protein.

Fusion proteins may generally be prepared using standard techniques, including chemical conjugation. Preferably, a fusion protein is expressed as a recombinant protein, allowing the production of increased levels, relative to a non-fused protein, in an expression system. Briefly,

10 DNA sequences encoding the polypeptide components may be assembled separately, and ligated into an appropriate expression vector. The 3' end of the DNA sequence encoding one polypeptide component is ligated, with or without a peptide linker, to the 5' end of a DNA sequence encoding the second polypeptide component so that the reading frames of the sequences are in phase. This permits translation into a single fusion protein that retains the biological activity of both component

15 polypeptides.

A peptide linker sequence may be employed to separate the first and the second polypeptide components by a distance sufficient to ensure that each polypeptide folds into its secondary and tertiary structures. Such a peptide linker sequence is incorporated into the fusion protein using standard techniques well known in the art. Suitable peptide linker sequences may be

20 chosen based on the following factors: (1) their ability to adopt a flexible extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker

25 sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene 40*:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA 83*:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may generally be from 1 to about 50 amino acids in length. Linker sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions

30 that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are

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located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons required to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, *336*:86-91, 1997).

Within preferred embodiments, an immunological fusion partner is derived from protein D, a surface protein of the gram-negative bacterium Haemophilus influenza B (WO 91/18926). Preferably, a protein D derivative comprises approximately the first third of the protein (*e.g.*, the first N-terminal 100-110 amino acids), and a protein D derivative may be lipidated. Within certain preferred embodiments, the first 109 residues of a Lipoprotein D fusion partner is included on the N-terminus to provide the polypeptide with additional exogenous T-cell epitopes and to increase the expression level in *E. coli* (thus functioning as an expression enhancer). The lipid tail ensures optimal presentation of the antigen to antigen presenting cells. Other fusion partners include the non-structural protein from influenzae virus, NS1 (hemaglutinin). Typically, the N-terminal 81 amino acids are used, although different fragments that include T-helper epitopes may be used.

In another embodiment, the immunological fusion partner is the protein known as LYTA, or a portion thereof (preferably a C-terminal portion). LYTA is derived from *Streptococcus pneumoniae*, which synthesizes an N-acetyl-L-alanine amidase known as amidase LYTA (encoded by the LytA gene; *Gene 43*:265-292, 1986). LYTA is an autolysin that specifically degrades certain bonds in the peptidoglycan backbone. The C-terminal domain of the LYTA protein is responsible for the affinity to the choline or to some choline analogues such as DEAE. This property has been exploited for the development of *E. coli* C-LYTA expressing plasmids useful for expression of fusion proteins. Purification of hybrid proteins containing the C-LYTA fragment at the amino terminus has been described (see *Biotechnology 10*:795-798, 1992). Within a preferred embodiment, a repeat portion of LYTA may be incorporated into a fusion protein. A repeat portion is found in the C-terminal region starting at residue 178. A particularly preferred repeat portion incorporates residues 188-305.

In general, polypeptides (including fusion proteins) and polynucleotides as described herein are isolated. An "isolated" polypeptide or polynucleotide is one that is removed from its

original environment. For example, a naturally-occurring protein is isolated if it is separated from some or all of the coexisting materials in the natural system. Preferably, such polypeptides are at least about 90% pure, more preferably at least about 95% pure and most preferably at least about 99% pure. A polynucleotide is considered to be isolated if, for example, it is cloned into a vector

5   that is not a part of the natural environment.

BINDING AGENTS

The present invention further provides agents, such as antibodies and antigen-binding fragments thereof, that specifically bind to a prostate-specific protein. As used herein, an

10 antibody, or antigen-binding fragment thereof, is said to "specifically bind" to a prostate-specific protein if it reacts at a detectable level (within, for example, an ELISA) with a prostate-specific protein, and does not react detectably with unrelated proteins under similar conditions. As used herein, "binding" refers to a noncovalent association between two separate molecules such that a complex is formed. The ability to bind may be evaluated by, for example, determining a binding

15 constant for the formation of the complex. The binding constant is the value obtained when the concentration of the complex is divided by the product of the component concentrations. In general, two compounds are said to "bind," in the context of the present invention, when the binding constant for complex formation exceeds about 10^3 L/mol. The binding constant may be determined using methods well known in the art.

20 Binding agents may be further capable of differentiating between patients with and without a cancer, such as prostate cancer, using the representative assays provided herein. In other words, antibodies or other binding agents that bind to a prostate-specific protein will generate a signal indicating the presence of a cancer in at least about 20% of patients with the disease, and will generate a negative signal indicating the absence of the disease in at least about 90% of individuals

25 without the cancer. To determine whether a binding agent satisfies this requirement, biological samples (e.g., blood, sera, urine and/or tumor biopsies) from patients with and without a cancer (as determined using standard clinical tests) may be assayed as described herein for the presence of polypeptides that bind to the binding agent. It will be apparent that a statistically significant number of samples with and without the disease should be assayed. Each binding agent should satisfy the

30 above criteria; however, those of ordinary skill in the art will recognize that binding agents may be used in combination to improve sensitivity.

Any agent that satisfies the above requirements may be a binding agent. For example, a binding agent may be a ribosome, with or without a peptide component, an RNA molecule or a polypeptide. In a preferred embodiment, a binding agent is an antibody or an antigen-binding fragment thereof. Most preferably, antibodies employed in the inventive methods have the ability to induce lysis of tumor cells by activation of complement and mediation of antibody-dependent cellular cytotoxicity (ADCC). Antibodies of different classes and subclasses differ in these properties. For example, mouse antibodies of the IgG2a and IgG3 classes are capable of activating serum complement upon binding to target cells which express the antigen against which the antibodies were raised, and can mediate ADCC.

Antibodies may be prepared by any of a variety of techniques known to those of ordinary skill in the art. *See, e.g.,* Harlow and Lane, *Antibodies: A Laboratory Manual,* Cold Spring Harbor Laboratory, 1988. In general, antibodies can be produced by cell culture techniques, including the generation of monoclonal antibodies as described herein, or via transfection of antibody genes into suitable bacterial or mammalian cell hosts, in order to allow for the production of recombinant antibodies. In one technique, an immunogen comprising the polypeptide is initially injected into any of a wide variety of mammals (*e.g.,* mice, rats, rabbits, sheep or goats). In this step, the polypeptides of this invention may serve as the immunogen without modification. Alternatively, particularly for relatively short polypeptides, a superior immune response may be elicited if the polypeptide is joined to a carrier protein, such as bovine serum albumin or keyhole limpet hemocyanin. The immunogen is injected into the animal host, preferably according to a predetermined schedule incorporating one or more booster immunizations, and the animals are bled periodically. Polyclonal antibodies specific for the polypeptide may then be purified from such antisera by, for example, affinity chromatography using the polypeptide coupled to a suitable solid support.

Monoclonal antibodies specific for an antigenic polypeptide of interest may be prepared, for example, using the technique of Kohler and Milstein, *Eur. J. Immunol.* 6:511-519, 1976, and improvements thereto. Briefly, these methods involve the preparation of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.,* reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells

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and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are

5   selected and their culture supernatants tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse.

10   Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

The preparation of mouse and rabbit monoclonal antibodies that specifically bind to

15   polypeptides of the present invention is described in detail below. However, the antibodies of the present invention are not limited to those derived from mice. Human antibodies may also be employed in the inventive methods and may prove to be preferable. Such antibodies can be obtained using human hybridomas as described by Cote *et al.* (Monoclonal Antibodies and Cancer Therapy, Alan R. Lisa, p. 77, 1985). The present invention also encompasses antibodies made by

20   recombinant means such as chimeric antibodies, wherein the variable region and constant region are derived from different species, and CDR-grafted antibodies, wherein the complementarity determining region is derived from a different species, as described in US Patents 4,816,567 and 5,225,539. Chimeric antibodies may be prepared by splicing genes for a mouse antibody molecule having a desired antigen specificity together with genes for a human antibody molecule having the

25   desired biological activity, such as activation of human complement and mediation of ADCC (Morrison *et al. Proc. Natl. Acad. Sci. USA 81*:6851, 1984; Neuberger *et al. Nature 312*:604, 1984; Takeda *et al. Nature 314*:452, 1985).

Within certain embodiments, the use of antigen-binding fragments of antibodies may be preferred. Such fragments include Fab fragments, which may be prepared using standard

30   techniques. Briefly, immunoglobulins may be purified from rabbit serum by affinity chromatography on Protein A bead columns (Harlow and Lane, *Antibodies: A Laboratory Manual,*

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Cold Spring Harbor Laboratory, 1988) and digested by papain to yield Fab and Fc fragments. The Fab and Fc fragments may be separated by affinity chromatography on protein A bead columns.

Monoclonal antibodies of the present invention may be coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers,

5   drugs, toxins, and derivatives thereof. Preferred radionuclides include ^{90}Y, ^{123}I, ^{125}I, ^{131}I, ^{186}Re, ^{188}Re, ^{211}At, and ^{212}Bi. Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diptheria toxin, cholera toxin, gelonin, Pseudomonas exotoxin, Shigella toxin, and pokeweed antiviral protein.

10 A therapeutic agent may be coupled (e.g., covalently bonded) to a suitable monoclonal antibody either directly or indirectly (e.g., via a linker group). A direct reaction between an agent and an antibody is possible when each possesses a substituent capable of reacting with the other. For example, a nucleophilic group, such as an amino or sulfhydryl group, on one may be capable of reacting with a carbonyl-containing group, such as an anhydride or an acid

15 halide, or with an alkyl group containing a good leaving group (e.g., a halide) on the other.

Alternatively, it may be desirable to couple a therapeutic agent and an antibody via a linker group. A linker group can function as a spacer to distance an antibody from an agent in order to avoid interference with binding capabilities. A linker group can also serve to increase the chemical reactivity of a substituent on an agent or an antibody, and thus increase the coupling

20 efficiency. An increase in chemical reactivity may also facilitate the use of agents, or functional groups on agents, which otherwise would not be possible.

It will be evident to those skilled in the art that a variety of bifunctional or polyfunctional reagents, both homo- and hetero-functional (such as those described in the catalog of the Pierce Chemical Co., Rockford, IL), may be employed as the linker group. Coupling may be

25 effected, for example, through amino groups, carboxyl groups, sulfhydryl groups or oxidized carbohydrate residues. There are numerous references describing such methodology, e.g., U.S. Patent No. 4,671,958, to Rodwell et al.

Where a therapeutic agent is more potent when free from the antibody portion of the immunoconjugates of the present invention, it may be desirable to use a linker group which is

30 cleavable during or upon internalization into a cell. A number of different cleavable linker groups have been described. The mechanisms for the intracellular release of an agent from these linker groups include cleavage by reduction of a disulfide bond (e.g., U.S. Patent No. 4,489,710, to

Spitler), by irradiation of a photolabile bond (*e.g.*, U.S. Patent No. 4,625,014, to Senter et al.), by hydrolysis of derivatized amino acid side chains (*e.g.*, U.S. Patent No. 4,638,045, to Kohn et al.), by serum complement-mediated hydrolysis (*e.g.*, U.S. Patent No. 4,671,958, to Rodwell et al.), and acid-catalyzed hydrolysis (*e.g.*, U.S. Patent No. 4,569,789, to Blattler et al.).

5   It may be desirable to couple more than one agent to an antibody. In one embodiment, multiple molecules of an agent are coupled to one antibody molecule. In another embodiment, more than one type of agent may be coupled to one antibody. Regardless of the particular embodiment, immunoconjugates with more than one agent may be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or

10   linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (*e.g.*, U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (*e.g.*, U.S. Patent

15   No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (*e.g.*, U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating

20   compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of

25   a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

T Cells

30   Immunotherapeutic compositions may also, or alternatively, comprise T cells specific for a prostate-specific protein. Such cells may generally be prepared *in vitro* or *ex vivo*, using standard procedures. For example, T cells may be isolated from bone marrow, peripheral

blood, or a fraction of bone marrow or peripheral blood of a patient, using a commercially available cell separation system, such as the ISOLEX™ system, available from Nexell Therapeutics Inc., Irvine, CA (see also U.S. Patent No. 5,240,856; U.S. Patent No. 5,215,926; WO 89/06280; WO 91/16116 and WO 92/07243). Alternatively, T cells may be derived from related or unrelated

5 humans, non-human mammals, cell lines or cultures.

T cells may be stimulated with a prostate-specific polypeptide, polynucleotide encoding a prostate-specific polypeptide and/or an antigen presenting cell (APC) that expresses such a polypeptide. Such stimulation is performed under conditions and for a time sufficient to permit the generation of T cells that are specific for the polypeptide. Preferably, a prostate-specific

10 polypeptide or polynucleotide is present within a delivery vehicle, such as a microsphere, to facilitate the generation of specific T cells.

T cells are considered to be specific for a prostate-specific polypeptide if the T cells specifically proliferate, secrete cytokines or kill target cells coated with the polypeptide or expressing a gene encoding the polypeptide. T cell specificity may be evaluated using any of a

15 variety of standard techniques. For example, within a chromium release assay or proliferation assay, a stimulation index of more than two fold increase in lysis and/or proliferation, compared to negative controls, indicates T cell specificity. Such assays may be performed, for example, as described in Chen et al., *Cancer Res.* *54*:1065-1070, 1994. Alternatively, detection of the proliferation of T cells may be accomplished by a variety of known techniques. For example, T cell

20 proliferation can be detected by measuring an increased rate of DNA synthesis (*e.g.,* by pulse-labeling cultures of T cells with tritiated thymidine and measuring the amount of tritiated thymidine incorporated into DNA). Contact with a prostate-specific polypeptide (100 ng/ml - 100 µg/ml, preferably 200 ng/ml - 25 µg/ml) for 3 - 7 days should result in at least a two fold increase in proliferation of the T cells. Contact as described above for 2-3 hours should result in activation of

25 the T cells, as measured using standard cytokine assays in which a two fold increase in the level of cytokine release (*e.g.,* TNF or IFN-γ) is indicative of T cell activation (*see* Coligan et al., Current Protocols in Immunology, vol. 1, Wiley Interscience (Greene 1998)). T cells that have been activated in response to a prostate-specific polypeptide, polynucleotide or polypeptide-expressing APC may be CD4+ and/or CD8+. Prostate-specific protein-specific T cells may be expanded using

30 standard techniques. Within preferred embodiments, the T cells are derived from either a patient or a related, or unrelated, donor and are administered to the patient following stimulation and expansion.

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For therapeutic purposes, CD4$^+$ or CD8$^+$ T cells that proliferate in response to a prostate-specific polypeptide, polynucleotide or APC can be expanded in number either *in vitro* or *in vivo*. Proliferation of such T cells *in vitro* may be accomplished in a variety of ways. For example, the T cells can be re-exposed to a prostate-specific polypeptide, or a short peptide

5   corresponding to an immunogenic portion of such a polypeptide, with or without the addition of T cell growth factors, such as interleukin-2, and/or stimulator cells that synthesize a prostate-specific polypeptide. Alternatively, one or more T cells that proliferate in the presence of a prostate-specific protein can be expanded in number by cloning. Methods for cloning cells are well known in the art, and include limiting dilution.

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PHARMACEUTICAL COMPOSITIONS AND VACCINES

Within certain aspects, polypeptides, polynucleotides, T cells and/or binding agents disclosed herein may be incorporated into pharmaceutical compositions or immunogenic compositions (*i.e.*, vaccines). Pharmaceutical compositions comprise one or more such compounds

15   and a physiologically acceptable carrier. Vaccines may comprise one or more such compounds and an immunostimulant. An immunostimulant may be any substance that enhances an immune response to an exogenous antigen. Examples of immunostimulants include adjuvants, biodegradable microspheres (*e.g.*, polylactic galactide) and liposomes (into which the compound is incorporated; *see e.g.*, Fullerton, U.S. Patent No. 4,235,877). Vaccine preparation is generally

20   described in, for example, M.F. Powell and M.J. Newman, eds., "Vaccine Design (the subunit and adjuvant approach)," Plenum Press (NY, 1995). Pharmaceutical compositions and vaccines within the scope of the present invention may also contain other compounds, which may be biologically active or inactive. For example, one or more immunogenic portions of other tumor antigens may be present, either incorporated into a fusion polypeptide or as a separate compound, within the

25   composition or vaccine.

A pharmaceutical composition or vaccine may contain DNA encoding one or more of the polypeptides as described above, such that the polypeptide is generated *in situ*. As noted above, the DNA may be present within any of a variety of delivery systems known to those of ordinary skill in the art, including nucleic acid expression systems, bacteria and viral expression

30   systems. Numerous gene delivery techniques are well known in the art, such as those described by Rolland, *Crit. Rev. Therap. Drug Carrier Systems 15*:143-198, 1998, and references cited therein. Appropriate nucleic acid expression systems contain the necessary DNA sequences for expression

in the patient (such as a suitable promoter and terminating signal). Bacterial delivery systems involve the administration of a bacterium (such as *Bacillus-Calmette-Guerrin*) that expresses an immunogenic portion of the polypeptide on its cell surface or secretes such an epitope. In a preferred embodiment, the DNA may be introduced using a viral expression system (*e.g.*, vaccinia

5 or other pox virus, retrovirus, or adenovirus), which may involve the use of a non-pathogenic (defective), replication competent virus. Suitable systems are disclosed, for example, in Fisher-Hoch et al., *Proc. Natl. Acad. Sci. USA 86*:317-321, 1989; Flexner et al., *Ann. N.Y. Acad. Sci. 569*:86-103, 1989; Flexner et al., *Vaccine 8*:17-21, 1990; U.S. Patent Nos. 4,603,112, 4,769,330, and 5,017,487; WO 89/01973; U.S. Patent No. 4,777,127; GB 2,200,651; EP 0,345,242;

10 WO 91/02805; Berkner, *Biotechniques 6*:616-627, 1988; Rosenfeld et al., *Science 252*:431-434, 1991; Kolls et al., *Proc. Natl. Acad. Sci. USA 91*:215-219, 1994; Kass-Eisler et al., *Proc. Natl. Acad. Sci. USA 90*:11498-11502, 1993; Guzman et al., *Circulation 88*:2838-2848, 1993; and Guzman et al., *Cir. Res. 73*:1202-1207, 1993. Techniques for incorporating DNA into such expression systems are well known to those of ordinary skill in the art. The DNA may also be

15 "naked," as described, for example, in Ulmer et al., *Science 259*:1745-1749, 1993 and reviewed by Cohen, *Science 259*:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported into the cells.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary

20 depending on the mode of administration. Compositions of the present invention may be formulated for any appropriate manner of administration, including for example, topical, oral, nasal, intravenous, intracranial, intraperitoneal, subcutaneous or intramuscular administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a fat, a wax or a buffer. For oral administration, any of the above carriers or a solid

25 carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and magnesium carbonate, may be employed. Biodegradable microspheres (*e.g.*, polylactate polyglycolate) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S. Patent Nos. 4,897,268 and 5,075,109.

30 Such compositions may also comprise buffers (*e.g.*, neutral buffered saline or phosphate buffered saline), carbohydrates (*e.g.*, glucose, mannose, sucrose or dextrans), mannitol, proteins, polypeptides or amino acids such as glycine, antioxidants, chelating agents such as EDTA

or glutathione, adjuvants (*e.g.*, aluminum hydroxide) and/or preservatives. Alternatively, compositions of the present invention may be formulated as a lyophilizate. Compounds may also be encapsulated within liposomes using well known technology.

Any of a variety of immunostimulants may be employed in the vaccines of this invention. For example, an adjuvant may be included. Most adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, *Bortadella pertussis* or *Mycobacterium tuberculosis* derived proteins. Suitable adjuvants are commercially available as, for example, Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A and quil A. Cytokines, such as GM-CSF or interleukin-2, -7, or -12, may also be used as adjuvants.

Within the vaccines provided herein, the adjuvant composition is preferably designed to induce an immune response predominantly of the Th1 type. High levels of Th1-type cytokines (*e.g.*, IFN-γ, TNFα, IL-2 and IL-12) tend to favor the induction of cell mediated immune responses to an administered antigen. In contrast, high levels of Th2-type cytokines (*e.g.*, IL-4, IL-5, IL-6 and IL-10) tend to favor the induction of humoral immune responses. Following application of a vaccine as provided herein, a patient will support an immune response that includes Th1- and Th2- type responses. Within a preferred embodiment, in which a response is predominantly Th1-type, the level of Th1-type cytokines will increase to a greater extent than the level of Th2-type cytokines. The levels of these cytokines may be readily assessed using standard assays. For a review of the families of cytokines, see Mosmann and Coffman, *Ann. Rev. Immunol.* 7:145-173, 1989.

Preferred adjuvants for use in eliciting a predominantly Th1-type response include, for example, a combination of monophosphoryl lipid A, preferably 3-de-O-acylated monophosphoryl lipid A (3D-MPL), together with an aluminum salt. MPL adjuvants are available from Ribi ImmunoChem Research Inc. (Hamilton, MT; *see* US Patent Nos. 4,436,727; 4,877,611; 4,866,034 and 4,912,094). CpG-containing oligonucleotides (in which the CpG dinucleotide is unmethylated) also induce a predominantly Th1 response. Such oligonucleotides are well known and are described, for example, in WO 96/02555. Another preferred adjuvant is a saponin, preferably QS21, which may be used alone or in combination with other adjuvants. For example,

an enhanced system involves the combination of a monophosphoryl lipid A and saponin derivative, such as the combination of QS21 and 3D-MPL as described in WO 94/00153, or a less reactogenic composition where the QS21 is quenched with cholesterol, as described in WO 96/33739. Other preferred formulations comprises an oil-in-water emulsion and tocopherol. A particularly potent

5   adjuvant formulation involving QS21, 3D-MPL and tocopherol in an oil-in-water emulsion is described in WO 95/17210. Any vaccine provided herein may be prepared using well known methods that result in a combination of antigen, immune response enhancer and a suitable carrier or excipient.

The compositions described herein may be administered as part of a sustained release

10   formulation (*i.e.*, a formulation such as a capsule, sponge or gel (composed of polysaccharides for example) that effects a slow release of compound following administration). Such formulations may generally be prepared using well known technology and administered by, for example, oral, rectal or subcutaneous implantation, or by implantation at the desired target site. Sustained-release formulations may contain a polypeptide, polynucleotide or antibody dispersed in a carrier matrix

15   and/or contained within a reservoir surrounded by a rate controlling membrane. Carriers for use within such formulations are biocompatible, and may also be biodegradable; preferably the formulation provides a relatively constant level of active component release. The amount of active compound contained within a sustained release formulation depends upon the site of implantation, the rate and expected duration of release and the nature of the condition to be treated or prevented.

20   Any of a variety of delivery vehicles may be employed within pharmaceutical compositions and vaccines to facilitate production of an antigen-specific immune response that targets tumor cells. Delivery vehicles include antigen presenting cells (APCs), such as dendritic cells, macrophages, B cells, monocytes and other cells that may be engineered to be efficient APCs. Such cells may, but need not, be genetically modified to increase the capacity for presenting the

25   antigen, to improve activation and/or maintenance of the T cell response, to have anti-tumor effects *per se* and/or to be immunologically compatible with the receiver (*i.e.*, matched HLA haplotype). APCs may generally be isolated from any of a variety of biological fluids and organs, including tumor and peritumoral tissues, and may be autologous, allogeneic, syngeneic or xenogeneic cells.

Certain preferred embodiments of the present invention use dendritic cells or

30   progenitors thereof as antigen-presenting cells. Dendritic cells are highly potent APCs (Banchereau and Steinman, *Nature 392*:245-251, 1998) and have been shown to be effective as a physiological adjuvant for eliciting prophylactic or therapeutic antitumor immunity (*see* Timmerman and Levy,

Ann. Rev. Med. 50:507-529, 1999). In general, dendritic cells may be identified based on their typical shape (stellate *in situ*, with marked cytoplasmic processes (dendrites) visible *in vitro*), their ability to take-up, process and present antigens with high efficiency, and their ability to activate naïve T cell responses. Dendritic cells may, of course, be engineered to express specific cell-surface

5   receptors or ligands that are not commonly found on dendritic cells *in vivo* or *ex vivo*, and such modified dendritic cells are contemplated by the present invention. As an alternative to dendritic cells, secreted vesicles antigen-loaded dendritic cells (called exosomes) may be used within a vaccine (*see* Zitvogel et al., *Nature Med. 4*:594-600, 1998).

Dendritic cells and progenitors may be obtained from peripheral blood, bone

10   marrow, tumor-infiltrating cells, peritumoral tissues-infiltrating cells, lymph nodes, spleen, skin, umbilical cord blood or any other suitable tissue or fluid. For example, dendritic cells may be differentiated *ex vivo* by adding a combination of cytokines such as GM-CSF, IL-4, IL-13 and/or TNFα to cultures of monocytes harvested from peripheral blood. Alternatively, CD34 positive cells harvested from peripheral blood, umbilical cord blood or bone marrow may be differentiated into

15   dendritic cells by adding to the culture medium combinations of GM-CSF, IL-3, TNFα, CD40 ligand, LPS, flt3 ligand and/or other compound(s) that induce differentiation, maturation and proliferation of dendritic cells.

Dendritic cells are conveniently categorized as "immature" and "mature" cells, which allows a simple way to discriminate between two well characterized phenotypes. However, this

20   nomenclature should not be construed to exclude all possible intermediate stages of differentiation. Immature dendritic cells are characterized as APC with a high capacity for antigen uptake and processing, which correlates with the high expression of Fcγ receptor and mannose receptor. The mature phenotype is typically characterized by a lower expression of these markers, but a high expression of cell surface molecules responsible for T cell activation such as class I and class II

25   MHC, adhesion molecules (*e.g.,* CD54 and CD11) and costimulatory molecules (*e.g.,* CD40, CD80, CD86 and 4-1BB).

APCs may generally be transfected with a polynucleotide encoding a prostate-specific protein (or portion or other variant thereof) such that the prostate-specific polypeptide, or an immunogenic portion thereof, is expressed on the cell surface. Such transfection may take place *ex*

30   *vivo*, and a composition or vaccine comprising such transfected cells may then be used for therapeutic purposes, as described herein. Alternatively, a gene delivery vehicle that targets a dendritic or other antigen presenting cell may be administered to a patient, resulting in transfection

that occurs *in vivo*. *In vivo* and *ex vivo* transfection of dendritic cells, for example, may generally be performed using any methods known in the art, such as those described in WO 97/24447, or the gene gun approach described by Mahvi et al., *Immunology and cell Biology 75*:456-460, 1997. Antigen loading of dendritic cells may be achieved by incubating dendritic cells or progenitor cells

5   with the prostate-specific polypeptide, DNA (naked or within a plasmid vector) or RNA; or with antigen-expressing recombinant bacterium or viruses (*e.g.*, vaccinia, fowlpox, adenovirus or lentivirus vectors). Prior to loading, the polypeptide may be covalently conjugated to an immunological partner that provides T cell help (*e.g.*, a carrier molecule). Alternatively, a dendritic cell may be pulsed with a non-conjugated immunological partner, separately or in the presence of

10 the polypeptide.

CANCER THERAPY

In further aspects of the present invention, the compositions described herein may be used for immunotherapy of cancer, such as prostate cancer. Within such methods, pharmaceutical

15 compositions and vaccines are typically administered to a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may or may not be afflicted with cancer. Accordingly, the above pharmaceutical compositions and vaccines may be used to prevent the development of a cancer or to treat a patient afflicted with a cancer. A cancer may be diagnosed using criteria generally accepted in the art, including the presence of a malignant tumor.

20 Pharmaceutical compositions and vaccines may be administered either prior to or following surgical removal of primary tumors and/or treatment such as administration of radiotherapy or conventional chemotherapeutic drugs.

Within certain embodiments, immunotherapy may be active immunotherapy, in which treatment relies on the *in vivo* stimulation of the endogenous host immune system to react

25 against tumors with the administration of immune response-modifying agents (such as polypeptides and polynucleotides disclosed herein).

Within other embodiments, immunotherapy may be passive immunotherapy, in which treatment involves the delivery of agents with established tumor-immune reactivity (such as effector cells or antibodies) that can directly or indirectly mediate antitumor effects and does not

30 necessarily depend on an intact host immune system. Examples of effector cells include T cells as discussed above, T lymphocytes (such as $CD8^+$ cytotoxic T lymphocytes and $CD4^+$ T-helper tumor-infiltrating lymphocytes), killer cells (such as Natural Killer cells and lymphokine-activated killer

cells), B cells and antigen-presenting cells (such as dendritic cells and macrophages) expressing a polypeptide provided herein. T cell receptors and antibody receptors specific for the polypeptides recited herein may be cloned, expressed and transferred into other vectors or effector cells for adoptive immunotherapy. The polypeptides provided herein may also be used to generate

5   antibodies or anti-idiotypic antibodies (as described above and in U.S. Patent No. 4,918,164) for passive immunotherapy.

Effector cells may generally be obtained in sufficient quantities for adoptive immunotherapy by growth *in vitro*, as described herein. Culture conditions for expanding single antigen-specific effector cells to several billion in number with retention of antigen recognition *in*

10   *vivo* are well known in the art. Such *in vitro* culture conditions typically use intermittent stimulation with antigen, often in the presence of cytokines (such as IL-2) and non-dividing feeder cells. As noted above, immunoreactive polypeptides as provided herein may be used to rapidly expand antigen-specific T cell cultures in order to generate a sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage, monocyte,

15   fibroblast or B cells, may be pulsed with immunoreactive polypeptides or transfected with one or more polynucleotides using standard techniques well known in the art. For example, antigen-presenting cells can be transfected with a polynucleotide having a promoter appropriate for increasing expression in a recombinant virus or other expression system. Cultured effector cells for use in therapy must be able to grow and distribute widely, and to survive long term *in vivo*. Studies

20   have shown that cultured effector cells can be induced to grow in vivo and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (*see*, for example, Cheever et al., *Immunological Reviews 157*:177, 1997).

Alternatively, a vector expressing a polypeptide recited herein may be introduced into antigen presenting cells taken from a patient and clonally propagated *ex vivo* for transplant back

25   into the same patient. Transfected cells may be reintroduced into the patient using any means known in the art, preferably in sterile form by intravenous, intracavitary, intraperitoneal or intratumor administration.

Routes and frequency of administration of the therapeutic compositions disclosed herein, as well as dosage, will vary from individual to individual, and may be readily established

30   using standard techniques. In general, the pharmaceutical compositions and vaccines may be administered by injection (*e.g.*, intracutaneous, intramuscular, intravenous or subcutaneous), intranasally (*e.g.*, by aspiration) or orally. Preferably, between 1 and 10 doses may be administered

over a 52 week period. Preferably, 6 doses are administered, at intervals of 1 month, and booster vaccinations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of a compound that, when administered as described above, is capable of promoting an anti-tumor immune response, and is at least 10-50%

5   above the basal (i.e., untreated) level. Such response can be monitored by measuring the anti-tumor antibodies in a patient or by vaccine-dependent generation of cytolytic effector cells capable of killing the patient's tumor cells in vitro. Such vaccines should also be capable of causing an immune response that leads to an improved clinical outcome (e.g., more frequent remissions, complete or partial or longer disease-free survival) in vaccinated patients as compared to non-

10   vaccinated patients. In general, for pharmaceutical compositions and vaccines comprising one or more polypeptides, the amount of each polypeptide present in a dose ranges from about 25 μg to 5 mg per kg of host. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.1 mL to about 5 mL.

In general, an appropriate dosage and treatment regimen provides the active

15   compound(s) in an amount sufficient to provide therapeutic and/or prophylactic benefit. Such a response can be monitored by establishing an improved clinical outcome (e.g., more frequent remissions, complete or partial, or longer disease-free survival) in treated patients as compared to non-treated patients. Increases in preexisting immune responses to a prostate-specific protein generally correlate with an improved clinical outcome. Such immune responses may generally be

20   evaluated using standard proliferation, cytotoxicity or cytokine assays, which may be performed using samples obtained from a patient before and after treatment.

METHODS FOR DETECTING CANCER

In general, a cancer may be detected in a patient based on the presence of one or

25   more prostate-specific proteins and/or polynucleotides encoding such proteins in a biological sample (for example, blood, sera, urine and/or tumor biopsies) obtained from the patient. In other words, such proteins may be used as markers to indicate the presence or absence of a cancer such as prostate cancer. In addition, such proteins may be useful for the detection of other cancers. The binding agents provided herein generally permit detection of the level of antigen that binds to the

30   agent in the biological sample. Polynucleotide primers and probes may be used to detect the level of mRNA encoding a tumor protein, which is also indicative of the presence or absence of a cancer.

In general, a prostate tumor sequence should be present at a level that is at least three fold higher in tumor tissue than in normal tissue

There are a variety of assay formats known to those of ordinary skill in the art for using a binding agent to detect polypeptide markers in a sample. *See, e.g.,* Harlow and Lane,
5 *Antibodies: A Laboratory Manual,* Cold Spring Harbor Laboratory, 1988. In general, the presence or absence of a cancer in a patient may be determined by (a) contacting a biological sample obtained from a patient with a binding agent; (b) detecting in the sample a level of polypeptide that binds to the binding agent; and (c) comparing the level of polypeptide with a predetermined cut-off value.

In a preferred embodiment, the assay involves the use of binding agent immobilized
10 on a solid support to bind to and remove the polypeptide from the remainder of the sample. The bound polypeptide may then be detected using a detection reagent that contains a reporter group and specifically binds to the binding agent/polypeptide complex. Such detection reagents may comprise, for example, a binding agent that specifically binds to the polypeptide or an antibody or other agent that specifically binds to the binding agent, such as an anti-immunoglobulin, protein G,
15 protein A or a lectin. Alternatively, a competitive assay may be utilized, in which a polypeptide is labeled with a reporter group and allowed to bind to the immobilized binding agent after incubation of the binding agent with the sample. The extent to which components of the sample inhibit the binding of the labeled polypeptide to the binding agent is indicative of the reactivity of the sample with the immobilized binding agent. Suitable polypeptides for use within such assays include full
20 length prostate-specific proteins and portions thereof to which the binding agent binds, as described above.

The solid support may be any material known to those of ordinary skill in the art to which the protein may be attached. For example, the solid support may be a test well in a microtiter plate or a nitrocellulose or other suitable membrane. Alternatively, the support may be a bead or
25 disc, such as glass, fiberglass, latex or a plastic material such as polystyrene or polyvinylchloride. The support may also be a magnetic particle or a fiber optic sensor, such as those disclosed, for example, in U.S. Patent No. 5,359,681. The binding agent may be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization"
30 refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the agent and functional groups on the support or may be a linkage by way of a cross-linking agent). Immobilization by adsorption to a well in a microtiter plate or to a

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membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of

5   binding agent ranging from about 10 ng to about 10 µg, and preferably about 100 ng to about 1 µg, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the

10   binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (see, e.g., Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

In certain embodiments, the assay is a two-antibody sandwich assay. This assay may

15   be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a detection reagent (preferably a second antibody capable of binding to a different site on the polypeptide) containing a reporter group is added. The

20   amount of detection reagent that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked. Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween

25   20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is then incubated with the sample, and polypeptide is allowed to bind to the antibody. The sample may be diluted with a suitable diluent, such as phosphate-buffered saline (PBS) prior to incubation. In general, an appropriate contact time (i.e., incubation time) is a period of time that is sufficient to detect the presence of polypeptide within a sample obtained from an individual with prostate cancer.

30   Preferably, the contact time is sufficient to achieve a level of binding that is at least about 95% of that achieved at equilibrium between bound and unbound polypeptide. Those of ordinary skill in the art will recognize that the time necessary to achieve equilibrium may be readily determined by

assaying the level of binding that occurs over a period of time. At room temperature, an incubation time of about 30 minutes is generally sufficient.

Unbound sample may then be removed by washing the solid support with an appropriate buffer, such as PBS containing 0.1% Tween 20™. The second antibody, which contains a reporter group, may then be added to the solid support. Preferred reporter groups include those groups recited above.

The detection reagent is then incubated with the immobilized antibody-polypeptide complex for an amount of time sufficient to detect the bound polypeptide. An appropriate amount of time may generally be determined by assaying the level of binding that occurs over a period of time. Unbound detection reagent is then removed and bound detection reagent is detected using the reporter group. The method employed for detecting the reporter group depends upon the nature of the reporter group. For radioactive groups, scintillation counting or autoradiographic methods are generally appropriate. Spectroscopic methods may be used to detect dyes, luminescent groups and fluorescent groups. Biotin may be detected using avidin, coupled to a different reporter group (commonly a radioactive or fluorescent group or an enzyme). Enzyme reporter groups may generally be detected by the addition of substrate (generally for a specific period of time), followed by spectroscopic or other analysis of the reaction products.

To determine the presence or absence of a cancer, such as prostate cancer, the signal detected from the reporter group that remains bound to the solid support is generally compared to a signal that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value for the detection of a cancer is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without the cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for the cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (*i.e.*, sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (*i.e.*, the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along

the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for a cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the binding agent is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized binding agent as the sample passes through the membrane. A second, labeled binding agent then binds to the binding agent-polypeptide complex as a solution containing the second binding agent flows through the membrane. The detection of bound second binding agent may then be performed as described above. In the strip test format, one end of the membrane to which binding agent is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second binding agent and to the area of immobilized binding agent. Concentration of second binding agent at the area of immobilized antibody indicates the presence of a cancer. Typically, the concentration of second binding agent at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of binding agent immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody sandwich assay, in the format discussed above. Preferred binding agents for use in such assays are antibodies and antigen-binding fragments thereof. Preferably, the amount of antibody immobilized on the membrane ranges from about 25 ng to about 1μg, and more preferably from about 50 ng to about 500 ng. Such tests can typically be performed with a very small amount of biological sample.

Of course, numerous other assay protocols exist that are suitable for use with the proteins or binding agents of the present invention. The above descriptions are intended to be exemplary only. For example, it will be apparent to those of ordinary skill in the art that the above protocols may be readily modified to use prostate-specific polypeptides to detect antibodies that bind to such polypeptides in a biological sample. The detection of such prostate-specific protein specific antibodies may correlate with the presence of a cancer.

A cancer may also, or alternatively, be detected based on the presence of T cells that specifically react with a prostate-specific protein in a biological sample. Within certain methods, a biological sample comprising $CD4^+$ and/or $CD8^+$ T cells isolated from a patient is incubated with a prostate-specific polypeptide, a polynucleotide encoding such a polypeptide and/or an APC that

expresses at least an immunogenic portion of such a polypeptide, and the presence or absence of specific activation of the T cells is detected. Suitable biological samples include, but are not limited to, isolated T cells. For example, T cells may be isolated from a patient by routine techniques (such as by Ficoll/Hypaque density gradient centrifugation of peripheral blood lymphocytes). T cells may
5   be incubated *in vitro* for 2-9 days (typically 4 days) at 37°C with prostate-specific polypeptide (*e.g.*, 5 - 25 μg/ml). It may be desirable to incubate another aliquot of a T cell sample in the absence of prostate-specific polypeptide to serve as a control. For CD4⁺ T cells, activation is preferably detected by evaluating proliferation of the T cells. For CD8⁺ T cells, activation is preferably detected by evaluating cytolytic activity. A level of proliferation that is at least two fold greater
10   and/or a level of cytolytic activity that is at least 20% greater than in disease-free patients indicates the presence of a cancer in the patient.

As noted above, a cancer may also, or alternatively, be detected based on the level of mRNA encoding a prostate-specific protein in a biological sample. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to
15   amplify a portion of a prostate-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for (*i.e.*, hybridizes to) a polynucleotide encoding the prostate-specific protein. The amplified cDNA is then separated and detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes that specifically hybridize to a polynucleotide encoding a prostate-specific protein may be used in a hybridization
20   assay to detect the presence of polynucleotide encoding the protein in a biological sample.

To permit hybridization under assay conditions, oligonucleotide primers and probes should comprise an oligonucleotide sequence that has at least about 60%, preferably at least about 75% and more preferably at least about 90%, identity to a portion of a polynucleotide encoding a prostate-specific protein that is at least 10 nucleotides, and preferably at least 20 nucleotides, in
25   length. Preferably, oligonucleotide primers and/or probes will hybridize to a polynucleotide encoding a polypeptide disclosed herein under moderately stringent conditions, as defined above. Oligonucleotide primers and/or probes which may be usefully employed in the diagnostic methods described herein preferably are at least 10-40 nucleotides in length. In a preferred embodiment, the oligonucleotide primers comprise at least 10 contiguous nucleotides, more preferably at least 15
30   contiguous nucleotides, of a DNA molecule having a sequence recited in SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382, 384-476, 524, 526, 530, 531, 533, 535 and 536. Techniques for both PCR based assays and hybridization assays

are well known in the art (*see*, for example, Mullis et al., *Cold Spring Harbor Symp. Quant. Biol.*, *51*:263, 1987; Erlich ed., *PCR Technology*, Stockton Press, NY, 1989).

One preferred assay employs RT-PCR, in which PCR is applied in conjunction with reverse transcription. Typically, RNA is extracted from a biological sample, such as biopsy tissue, and is reverse transcribed to produce cDNA molecules. PCR amplification using at least one specific primer generates a cDNA molecule, which may be separated and visualized using, for example, gel electrophoresis. Amplification may be performed on biological samples taken from a test patient and from an individual who is not afflicted with a cancer. The amplification reaction may be performed on several dilutions of cDNA spanning two orders of magnitude. A two-fold or greater increase in expression in several dilutions of the test patient sample as compared to the same dilutions of the non-cancerous sample is typically considered positive.

In another embodiment, the disclosed compositions may be used as markers for the progression of cancer. In this embodiment, assays as described above for the diagnosis of a cancer may be performed over time, and the change in the level of reactive polypeptide(s) or polynucleotide evaluated. For example, the assays may be performed every 24-72 hours for a period of 6 months to 1 year, and thereafter performed as needed. In general, a cancer is progressing in those patients in whom the level of polypeptide or polynucleotide detected increases over time. In contrast, the cancer is not progressing when the level of reactive polypeptide or polynucleotide either remains constant or decreases with time.

Certain *in vivo* diagnostic assays may be performed directly on a tumor. One such assay involves contacting tumor cells with a binding agent. The bound binding agent may then be detected directly or indirectly via a reporter group. Such binding agents may also be used in histological applications. Alternatively, polynucleotide probes may be used within such applications.

As noted above, to improve sensitivity, multiple prostate-specific protein markers may be assayed within a given sample. It will be apparent that binding agents specific for different proteins provided herein may be combined within a single assay. Further, multiple primers or probes may be used concurrently. The selection of protein markers may be based on routine experiments to determine combinations that results in optimal sensitivity. In addition, or alternatively, assays for proteins provided herein may be combined with assays for other known tumor antigens.

DIAGNOSTIC KITS

The present invention further provides kits for use within any of the above diagnostic methods. Such kits typically comprise two or more components necessary for performing a diagnostic assay. Components may be compounds, reagents, containers and/or equipment. For example, one container within a kit may contain a monoclonal antibody or fragment thereof that specifically binds to a prostate-specific protein. Such antibodies or fragments may be provided attached to a support material, as described above. One or more additional containers may enclose elements, such as reagents or buffers, to be used in the assay. Such kits may also, or alternatively, contain a detection reagent as described above that contains a reporter group suitable for direct or indirect detection of antibody binding.

Alternatively, a kit may be designed to detect the level of mRNA encoding a prostate-specific protein in a biological sample. Such kits generally comprise at least one oligonucleotide probe or primer, as described above, that hybridizes to a polynucleotide encoding a prostate-specific protein. Such an oligonucleotide may be used, for example, within a PCR or hybridization assay. Additional components that may be present within such kits include a second oligonucleotide and/or a diagnostic reagent or container to facilitate the detection of a polynucleotide encoding a prostate-specific protein.

The following Examples are offered by way of illustration and not by way of limitation.

<u>EXAMPLES</u>

EXAMPLE 1

5   ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES

This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library was constructed from prostate

10   tumor poly A$^+$ RNA using a Superscript Plasmid System for cDNA Synthesis and Plasmid Cloning kit (BRL Life Technologies, Gaithersburg, MD 20897) following the manufacturer's protocol. Specifically, prostate tumor tissues were homogenized with polytron (Kinematica, Switzerland) and total RNA was extracted using Trizol reagent (BRL Life Technologies) as directed by the manufacturer. The poly A$^+$ RNA was then purified using a Qiagen oligotex spin column mRNA

15   purification kit (Qiagen, Santa Clarita, CA 91355) according to the manufacturer's protocol. First-strand cDNA was synthesized using the NotI/Oligo-dT18 primer. Double-stranded cDNA was synthesized, ligated with EcoRI/BAXI adaptors (Invitrogen, San Diego, CA) and digested with NotI. Following size fractionation with Chroma Spin-1000 columns (Clontech, Palo Alto, CA), the cDNA was ligated into the EcoRI/NotI site of pCDNA3.1 (Invitrogen) and transformed into

20   ElectroMax *E. coli* DH10B cells (BRL Life Technologies) by electroporation.

Using the same procedure, a normal human pancreas cDNA expression library was prepared from a pool of six tissue specimens (Clontech). The cDNA libraries were characterized by determining the number of independent colonies, the percentage of clones that carried insert, the average insert size and by sequence analysis. The prostate tumor library contained 1.64 x 10^7

25   independent colonies, with 70% of clones having an insert and the average insert size being 1745 base pairs. The normal pancreas cDNA library contained 3.3 x 10^6 independent colonies, with 69% of clones having inserts and the average insert size being 1120 base pairs. For both libraries, sequence analysis showed that the majority of clones had a full length cDNA sequence and were synthesized from mRNA, with minimal rRNA and mitochondrial DNA contamination.

30   cDNA library subtraction was performed using the above prostate tumor and normal pancreas cDNA libraries, as described by Hara *et al.* (*Blood, 84*:189-199, 1994) with some modifications. Specifically, a prostate tumor-specific subtracted cDNA library was generated as

follows. Normal pancreas cDNA library (70 μg) was digested with EcoRI, NotI, and SfuI, followed by a filling-in reaction with DNA polymerase Klenow fragment. After phenol-chloroform extraction and ethanol precipitation, the DNA was dissolved in 100 μl of H_2O, heat-denatured and mixed with 100 μl (100 μg) of Photoprobe biotin (Vector Laboratories, Burlingame, CA). As

5   recommended by the manufacturer, the resulting mixture was irradiated with a 270 W sunlamp on ice for 20 minutes. Additional Photoprobe biotin (50 μl) was added and the biotinylation reaction was repeated. After extraction with butanol five times, the DNA was ethanol-precipitated and dissolved in 23 μl H_2O to form the driver DNA.

To form the tracer DNA, 10 μg prostate tumor cDNA library was digested with

10   BamHI and XhoI, phenol chloroform extracted and passed through Chroma spin-400 columns (Clontech). Following ethanol precipitation, the tracer DNA was dissolved in 5 μl H_2O. Tracer DNA was mixed with 15 μl driver DNA and 20 μl of 2 x hybridization buffer (1.5 M NaCl/10 mM EDTA/50 mM HEPES pH 7.5/0.2% sodium dodecyl sulfate), overlaid with mineral oil, and heat-denatured completely. The sample was immediately transferred into a 68 °C water bath and

15   incubated for 20 hours (long hybridization [LH]). The reaction mixture was then subjected to a streptavidin treatment followed by phenol/chloroform extraction. This process was repeated three more times. Subtracted DNA was precipitated, dissolved in 12 μl H_2O, mixed with 8 μl driver DNA and 20 μl of 2 x hybridization buffer, and subjected to a hybridization at 68 °C for 2 hours (short hybridization [SH]). After removal of biotinylated double-stranded DNA, subtracted cDNA

20   was ligated into BamHI/XhoI site of chloramphenicol resistant pBCSK⁺ (Stratagene, La Jolla, CA 92037) and transformed into ElectroMax *E. coli* DH10B cells by electroporation to generate a prostate tumor specific subtracted cDNA library (referred to as "prostate subtraction 1").

To analyze the subtracted cDNA library, plasmid DNA was prepared from 100 independent clones, randomly picked from the subtracted prostate tumor specific library and

25   grouped based on insert size. Representative cDNA clones were further characterized by DNA sequencing with a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A (Foster City, CA). Six cDNA clones, hereinafter referred to as F1-13, F1-12, F1-16, H1-1, H1-9 and H1-4, were shown to be abundant in the subtracted prostate-specific cDNA library. The determined 3' and 5' cDNA sequences for F1-12 are provided in SEQ ID NO: 2 and 3, respectively,

30   with determined 3' cDNA sequences for F1-13, F1-16, H1-1, H1-9 and H1-4 being provided in SEQ ID NO: 1 and 4-7, respectively.

The cDNA sequences for the isolated clones were compared to known sequences in the gene bank using the EMBL and GenBank databases (release 96). Four of the prostate tumor cDNA clones, F1-13, F1-16, H1-1, and H1-4, were determined to encode the following previously identified proteins: prostate specific antigen (PSA), human glandular kallikrein, human tumor expression enhanced gene, and mitochondria cytochrome C oxidase subunit II. H1-9 was found to be identical to a previously identified human autonomously replicating sequence. No significant homologies to the cDNA sequence for F1-12 were found.

Subsequent studies led to the isolation of a full-length cDNA sequence for F1-12. This sequence is provided in SEQ ID NO: 107, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 108.

To clone less abundant prostate tumor specific genes, cDNA library subtraction was performed by subtracting the prostate tumor cDNA library described above with the normal pancreas cDNA library and with the three most abundant genes in the previously subtracted prostate tumor specific cDNA library: human glandular kallikrein, prostate specific antigen (PSA), and mitochondria cytochrome C oxidase subunit II. Specifically, 1 μg each of human glandular kallikrein, PSA and mitochondria cytochrome C oxidase subunit II cDNAs in pCDNA3.1 were added to the driver DNA and subtraction was performed as described above to provide a second subtracted cDNA library hereinafter referred to as the "subtracted prostate tumor specific cDNA library with spike".

Twenty-two cDNA clones were isolated from the subtracted prostate tumor specific cDNA library with spike. The determined 3' and 5' cDNA sequences for the clones referred to as J1-17, L1-12, N1-1862, J1-13, J1-19, J1-25, J1-24, K1-58, K1-63, L1-4 and L1-14 are provided in SEQ ID NOS: 8-9, 10-11, 12-13, 14-15, 16-17, 18-19, 20-21, 22-23, 24-25, 26-27 and 28-29, respectively. The determined 3' cDNA sequences for the clones referred to as J1-12, J1-16, J1-21, K1-48, K1-55, L1-2, L1-6, N1-1858, N1-1860, N1-1861, N1-1864 are provided in SEQ ID NOS: 30-40, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to three of the five most abundant DNA species, (J1-17, L1-12 and N1-1862; SEQ ID NOS: 8-9, 10-11 and 12-13, respectively). Of the remaining two most abundant species, one (J1-12; SEQ ID NO:30) was found to be identical to the previously identified human pulmonary surfactant-associated protein, and the other (K1-48; SEQ ID NO:33) was determined to have some homology to R. norvegicus mRNA for 2-arylpropionyl-CoA epimerase. Of the 17 less abundant cDNA clones isolated from the subtracted prostate tumor specific cDNA

library with spike, four (J1-16, K1-55, L1-6 and N1-1864; SEQ ID NOS:31, 34, 36 and 40, respectively) were found to be identical to previously identified sequences, two (J1-21 and N1-1860; SEQ ID NOS: 32 and 38, respectively) were found to show some homology to non-human sequences, and two (L1-2 and N1-1861; SEQ ID NOS: 35 and 39, respectively) were found to show

5   some homology to known human sequences. No significant homologies were found to the polypeptides J1-13, J1-19, J1-24, J1-25, K1-58, K1-63, L1-4, L1-14 (SEQ ID NOS: 14-15, 16-17, 20-21, 18-19, 22-23, 24-25, 26-27, 28-29, respectively).

Subsequent studies led to the isolation of full length cDNA sequences for J1-17, L1-12 and N1-1862 (SEQ ID NOS: 109-111, respectively). The corresponding predicted amino acid

10 sequences are provided in SEQ ID NOS: 112-114. L1-12 is also referred to as P501S.

In a further experiment, four additional clones were identified by subtracting a prostate tumor cDNA library with normal prostate cDNA prepared from a pool of three normal prostate poly A+ RNA (referred to as "prostate subtraction 2"). The determined cDNA sequences for these clones, hereinafter referred to as U1-3064, U1-3065, V1-3692 and 1A-3905, are provided

15 in SEQ ID NO: 69-72, respectively. Comparison of the determined sequences with those in the gene bank revealed no significant homologies to U1-3065.

A second subtraction with spike (referred to as "prostate subtraction spike 2") was performed by subtracting a prostate tumor specific cDNA library with spike with normal pancreas cDNA library and further spiked with PSA, J1-17, pulmonary surfactant-associated protein,

20 mitochondrial DNA, cytochrome c oxidase subunit II, N1-1862, autonomously replicating sequence, L1-12 and tumor expression enhanced gene. Four additional clones, hereinafter referred to as V1-3686, R1-2330, 1B-3976 and V1-3679, were isolated. The determined cDNA sequences for these clones are provided in SEQ ID NO:73-76, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to V1-3686 and R1-2330.

25 Further analysis of the three prostate subtractions described above (prostate subtraction 2, subtracted prostate tumor specific cDNA library with spike, and prostate subtraction spike 2) resulted in the identification of sixteen additional clones, referred to as 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1G-4734, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4810, 1I-4811, 1J-4876, 1K-4884 and 1K-4896. The determined cDNA sequences for these clones are provided in

30 SEQ ID NOS: 77-92, respectively. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to 1G-4741, 1G-4734, 1I-4807, 1J-4876 and 1K-4896 (SEQ ID NOS: 79, 81, 87, 90 and 92, respectively). Further analysis of the isolated

clones led to the determination of extended cDNA sequences for 1G-4736, 1G-4738, 1G-4741, 1G-4744, 1H-4774, 1H-4781, 1H-4785, 1H-4787, 1H-4796, 1I-4807, 1J-4876, 1K-4884 and 1K-4896, provided in SEQ ID NOS: 179-188 and 191-193, respectively, and to the determination of additional partial cDNA sequences for 1I-4810 and 1I-4811, provided in SEQ ID NOS: 189 and 190, respectively.

Additional studies with prostate subtraction spike 2 resulted in the isolation of three more clones. Their sequences were determined as described above and compared to the most recent GenBank. All three clones were found to have homology to known genes, which are Cysteine-rich protein, KIAA0242, and KIAA0280 (SEQ ID NO: 317, 319, and 320, respectively). Further analysis of these clones by Synteni microarray (Synteni, Palo Alto, CA) demonstrated that all three clones were over-expressed in most prostate tumors and prostate BPH, as well as in the majority of normal prostate tissues tested, but low expression in all other normal tissues.

An additional subtraction was performed by subtracting a normal prostate cDNA library with normal pancreas cDNA (referred to as "prostate subtraction 3"). This led to the identification of six additional clones referred to as 1G-4761, 1G-4762, 1H-4766, 1H-4770, 1H-4771 and 1H-4772 (SEQ ID NOS: 93-98). Comparison of these sequences with those in the gene bank revealed no significant homologies to 1G-4761 and 1H-4771 (SEQ ID NOS: 93 and 97, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1G-4761, 1G-4762, 1H-4766 and 1H-4772 provided in SEQ ID NOS: 194-196 and 199, respectively, and to the determination of additional partial cDNA sequences for 1H-4770 and 1H-4771, provided in SEQ ID NOS: 197 and 198, respectively.

Subtraction of a prostate tumor cDNA library, prepared from a pool of polyA+ RNA from three prostate cancer patients, with a normal pancreas cDNA library (prostate subtraction 4) led to the identification of eight clones, referred to as 1D-4297, 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280 (SEQ ID NOS: 99-107). These sequences were compared to those in the gene bank as described above. No significant homologies were found to 1D-4283 and 1D-4304 (SEQ ID NOS: 103 and 104, respectively). Further analysis of the isolated clones led to the determination of extended cDNA sequences for 1D-4309, 1D.1-4278, 1D-4288, 1D-4283, 1D-4304, 1D-4296 and 1D-4280, provided in SEQ ID NOS: 200-206, respectively.

cDNA clones isolated in prostate subtraction 1 and prostate subtraction 2, described above, were colony PCR amplified and their mRNA expression levels in prostate tumor, normal prostate and in various other normal tissues were determined using microarray technology (Synteni,

Palo Alto, CA). Briefly, the PCR amplification products were dotted onto slides in an array format, with each product occupying a unique location in the array. mRNA was extracted from the tissue sample to be tested, reverse transcribed, and fluorescent-labeled cDNA probes were generated. The microarrays were probed with the labeled cDNA probes, the slides scanned and fluorescence

5   intensity was measured. This intensity correlates with the hybridization intensity. Two clones (referred to as P509S and P510S) were found to be over-expressed in prostate tumor and normal prostate and expressed at low levels in all other normal tissues tested (liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon). The determined cDNA sequences for P509S and

10   P510S are provided in SEQ ID NO: 223 and 224, respectively. Comparison of these sequences with those in the gene bank as described above, revealed some homology to previously identified ESTs.

Additional, studies led to the isolation of the full-length cDNA sequence for P509S. This sequence is provided in SEQ ID NO: 332, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 339. Two variant full-length cDNA sequences for P510S

15   are provided in SEQ ID NO: 535 and 536, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 537 and 538, respectively.

EXAMPLE 2

DETERMINATION OF TISSUE SPECIFICITY OF PROSTATE-SPECIFIC POLYPEPTIDES

20   Using gene specific primers, mRNA expression levels for the representative prostate-specific polypeptides F1-16, H1-1, J1-17 (also referred to as P502S), L1-12 (also referred to as P501S), F1-12 (also referred to as P504S) and N1-1862 (also referred to as P503S) were examined in a variety of normal and tumor tissues using RT-PCR.

Briefly, total RNA was extracted from a variety of normal and tumor tissues using

25   Trizol reagent as described above. First strand synthesis was carried out using 1-2 μg of total RNA with SuperScript II reverse transcriptase (BRL Life Technologies) at 42 °C for one hour. The cDNA was then amplified by PCR with gene-specific primers. To ensure the semi-quantitative nature of the RT-PCR, β-actin was used as an internal control for each of the tissues examined. First, serial dilutions of the first strand cDNAs were prepared and RT-PCR assays were performed

30   using β-actin specific primers. A dilution was then chosen that enabled the linear range amplification of the β-actin template and which was sensitive enough to reflect the differences in the initial copy numbers. Using these conditions, the β-actin levels were determined for each

reverse transcription reaction from each tissue. DNA contamination was minimized by DNase treatment and by assuring a negative PCR result when using first strand cDNA that was prepared without adding reverse transcriptase.

mRNA Expression levels were examined in four different types of tumor tissue (prostate tumor from 2 patients, breast tumor from 3 patients, colon tumor, lung tumor), and sixteen different normal tissues, including prostate, colon, kidney, liver, lung, ovary, pancreas, skeletal muscle, skin, stomach, testes, bone marrow and brain. F1-16 was found to be expressed at high levels in prostate tumor tissue, colon tumor and normal prostate, and at lower levels in normal liver, skin and testes, with expression being undetectable in the other tissues examined. H1-1 was found to be expressed at high levels in prostate tumor, lung tumor, breast tumor, normal prostate, normal colon and normal brain, at much lower levels in normal lung, pancreas, skeletal muscle, skin, small intestine, bone marrow, and was not detected in the other tissues tested. J1-17 (P502S) and L1-12 (P501S) appear to be specifically over-expressed in prostate, with both genes being expressed at high levels in prostate tumor and normal prostate but at low to undetectable levels in all the other tissues examined. N1-1862 (P503S) was found to be over-expressed in 60% of prostate tumors and detectable in normal colon and kidney. The RT-PCR results thus indicate that F1-16, H1-1, J1-17 (P502S), N1-1862 (P503S) and L1-12 (P501S) are either prostate specific or are expressed at significantly elevated levels in prostate.

Further RT-PCR studies showed that F1-12 (P504S) is over-expressed in 60% of prostate tumors, detectable in normal kidney but not detectable in all other tissues tested. Similarly, R1-2330 was shown to be over-expressed in 40% of prostate tumors, detectable in normal kidney and liver, but not detectable in all other tissues tested. U1-3064 was found to be over-expressed in 60% of prostate tumors, and also expressed in breast and colon tumors, but was not detectable in normal tissues.

RT-PCR characterization of R1-2330, U1-3064 and 1D-4279 showed that these three antigens are over-expressed in prostate and/or prostate tumors.

Northern analysis with four prostate tumors, two normal prostate samples, two BPH prostates, and normal colon, kidney, liver, lung, pancrease, skeletal muscle, brain, stomach, testes, small intestine and bone marrow, showed that L1-12 (P501S) is over-expressed in prostate tumors and normal prostate, while being undetectable in other normal tissues tested. J1-17 (P502S) was detected in two prostate tumors and not in the other tissues tested. N1-1862 (P503S) was found to be over-expressed in three prostate tumors and to be expressed in normal prostate, colon and kidney,

but not in other tissues tested. F1-12 (P504S) was found to be highly expressed in two prostate tumors and to be undetectable in all other tissues tested.

The microarray technology described above was used to determine the expression levels of representative antigens described herein in prostate tumor, breast tumor and the following 5 normal tissues: prostate, liver, pancreas, skin, bone marrow, brain, breast, adrenal gland, bladder, testes, salivary gland, large intestine, kidney, ovary, lung, spinal cord, skeletal muscle and colon. L1-12 (P501S) was found to be over-expressed in normal prostate and prostate tumor, with some expression being detected in normal skeletal muscle. Both J1-12 and F1-12 (P504S) were found to be over-expressed in prostate tumor, with expression being lower or undetectable in all other tissues 10 tested. N1-1862 (P503S) was found to be expressed at high levels in prostate tumor and normal prostate, and at low levels in normal large intestine and normal colon, with expression being undetectable in all other tissues tested. R1-2330 was found to be over-expressed in prostate tumor and normal prostate, and to be expressed at lower levels in all other tissues tested. 1D-4279 was found to be over-expressed in prostate tumor and normal prostate, expressed at lower levels in ‾ 15 normal spinal cord, and to be undetectable in all other tissues tested.

Further microarray analysis to specifically address the extent to which P501S (SEQ ID NO: 110) was expressed in breast tumor revealed moderate over-expression not only in breast tumor, but also in metastatic breast tumor (2/31), with negligible to low expression in normal tissues. This data suggests that P501S may be over-expressed in various breast tumors as well as in 20 prostate tumors.

The expression levels of 32 ESTs (expressed sequence tags) described by Vasmatzis et al. (Proc. Natl. Acad. Sci. USA 95:300-304, 1998) in a variety of tumor and normal tissues were examined by microarray technology as described above. Two of these clones (referred to as P1000C and P1001C) were found to be over-expressed in prostate tumor and normal prostate, and 25 expressed at low to undetectable levels in all other tissues tested (normal aorta, thymus, resting and activated PBMC, epithelial cells, spinal cord, adrenal gland, fetal tissues, skin, salivary gland, large intestine, bone marrow, liver, lung, dendritic cells, stomach, lymph nodes, brain, heart, small intestine, skeletal muscle, colon and kidney. The determined cDNA sequences for P1000C and P1001C are provided in SEQ ID NO: 384 and 472, respectively. The sequence of P1001C was 30 found to show some homology to the previously isolated Human mRNA for JM27 protein. No significant homologies were found to the sequence of P1000C.

The expression of the polypeptide encoded by the full length cDNA sequence for F1-12 (also referred to as P504S; SEQ ID NO: 108) was investigated by immunohistochemical analysis. Rabbit-anti-P504S polyclonal antibodies were generated against the full length P504S protein by standard techniques. Subsequent isolation and characterization of the polyclonal antibodies were also performed by techniques well known in the art. Immunohistochemical analysis showed that the P504S polypeptide was expressed in 100% of prostate carcinoma samples tested (n=5).

The rabbit-anti-P504S polyclonal antibody did not appear to label benign prostate cells with the same cytoplasmic granular staining, but rather with light nuclear staining. Analysis of normal tissues revealed that the encoded polypeptide was found to be expressed in some, but not all normal human tissues. Positive cytoplasmic staining with rabbit-anti-P504S polyclonal antibody was found in normal human kidney, liver, brain, colon and lung-associated macrophages, whereas heart and bone marrow were negative.

This data indicates that the P504S polypeptide is present in prostate cancer tissues, and that there are qualitative and quantitative differences in the staining between benign prostatic hyperplasia tissues and prostate cancer tissues, suggesting that this polypeptide may be detected selectively in prostate tumors and therefore be useful in the diagnosis of prostate cancer.

EXAMPLE 3

ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

A cDNA subtraction library, containing cDNA from normal prostate subtracted with ten other normal tissue cDNAs (brain, heart, kidney, liver, lung, ovary, placenta, skeletal muscle, spleen and thymus) and then submitted to a first round of PCR amplification, was purchased from Clontech. This library was subjected to a second round of PCR amplification, following the manufacturer's protocol. The resulting cDNA fragments were subcloned into the vector pT7 Blue T-vector (Novagen, Madison, WI) and transformed into XL-1 Blue MRF' *E. coli* (Stratagene). DNA was isolated from independent clones and sequenced using a Perkin Elmer/Applied Biosystems Division Automated Sequencer Model 373A.

Fifty-nine positive clones were sequenced. Comparison of the DNA sequences of these clones with those in the gene bank, as described above, revealed no significant homologies to 25 of these clones, hereinafter referred to as P5, P8, P9, P18, P20, P30, P34, P36, P38, P39, P42, P49, P50, P53, P55, P60, P64, P65, P73, P75, P76, P79 and P84. The determined cDNA sequences

5 for these clones are provided in SEQ ID NO: 41-45, 47-52 and 54-65, respectively. P29, P47, P68, P80 and P82 (SEQ ID NO: 46, 53 and 66-68, respectively) were found to show some degree of homology to previously identified DNA sequences. To the best of the inventors' knowledge, none of these sequences have been previously shown to be present in prostate.

Further studies using the PCR-based methodology described above resulted in the

10 isolation of more than 180 additional clones, of which 23 clones were found to show no significant homologies to known sequences. The determined cDNA sequences for these clones are provided in SEQ ID NO: 115-123, 127, 131, 137, 145, 147-151, 153, 156-158 and 160. Twenty-three clones (SEQ ID NO: 124-126, 128-130, 132-136, 138-144, 146, 152, 154, 155 and 159) were found to show some homology to previously identified ESTs. An additional ten clones (SEQ ID NO: 161-

15 170) were found to have some degree of homology to known genes. Larger cDNA clones containing the P20 sequence represent splice variants of a gene referred to as P703P. The determined DNA sequence for the variants referred to as DE1, DE13 and DE14 are provided in SEQ ID NOS: 171, 175 and 177, respectively, with the corresponding predicted amino acid sequences being provided in SEQ ID NO: 172, 176 and 178, respectively. The determined cDNA

20 sequence for an extended spliced form of P703 is provided in SEQ ID NO: 225. The DNA sequences for the splice variants referred to as DE2 and DE6 are provided in SEQ ID NOS: 173 and 174, respectively.

mRNA Expression levels for representative clones in tumor tissues (prostate (n=5), breast (n=2), colon and lung) normal tissues (prostate (n=5), colon, kidney, liver, lung (n=2), ovary

25 (n=2), skeletal muscle, skin, stomach, small intestine and brain), and activated and non-activated PBMC was determined by RT-PCR as described above. Expression was examined in one sample of each tissue type unless otherwise indicated.

P9 was found to be highly expressed in normal prostate and prostate tumor compared to all normal tissues tested except for normal colon which showed comparable expression. P20, a

30 portion of the P703P gene, was found to be highly expressed in normal prostate and prostate tumor, compared to all twelve normal tissues tested. A modest increase in expression of P20 in breast tumor (n=2), colon tumor and lung tumor was seen compared to all normal tissues except lung (1 of

2). Increased expression of P18 was found in normal prostate, prostate tumor and breast tumor compared to other normal tissues except lung and stomach. A modest increase in expression of P5 was observed in normal prostate compared to most other normal tissues. However, some elevated expression was seen in normal lung and PBMC. Elevated expression of P5 was also observed in

5 prostate tumors (2 of 5), breast tumor and one lung tumor sample. For P30, similar expression levels were seen in normal prostate and prostate tumor, compared to six of twelve other normal tissues tested. Increased expression was seen in breast tumors, one lung tumor sample and one colon tumor sample, and also in normal PBMC. P29 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to the majority of normal tissues. However,

10 substantial expression of P29 was observed in normal colon and normal lung (2 of 2). P80 was found to be over-expressed in prostate tumor (5 of 5) and normal prostate (5 of 5) compared to all other normal tissues tested, with increased expression also being seen in colon tumor.

Further studies resulted in the isolation of twelve additional clones, hereinafter referred to as 10-d8, 10-h10, 11-c8, 7-g6, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3, 8-h11, 9-f12 and 9-f3. The

15 determined DNA sequences for 10-d8, 10-h10, 11-c8, 8-d4, 8-d9, 8-h11, 9-f12 and 9-f3 are provided in SEQ ID NO: 207, 208, 209, 216, 217, 220, 221 and 222, respectively. The determined forward and reverse DNA sequences for 7-g6, 8-b5, 8-b6 and 8-g3 are provided in SEQ ID NO: 210 and 211; 212 and 213; 214 and 215; and 218 and 219, respectively. Comparison of these sequences with those in the gene bank revealed no significant homologies to the sequence of 9-f3. The clones

20 10-d8, 11-c8 and 8-h11 were found to show some homology to previously isolated ESTs, while 10-h10, 8-b5, 8-b6, 8-d4, 8-d9, 8-g3 and 9-f12 were found to show some homology to previously identified genes. Further characterization of 7-G6 and 8-G3 showed identity to the known genes PAP and PSA, respectively.

mRNA expression levels for these clones were determined using the micro-array

25 technology described above. The clones 7-G6, 8-G3, 8-B5, 8-B6, 8-D4, 8-D9, 9-F3, 9-F12, 9-H3, 10-A2, 10-A4, 11-C9 and 11-F2 were found to be over-expressed in prostate tumor and normal prostate, with expression in other tissues tested being low or undetectable. Increased expression of 8-F11 was seen in prostate tumor and normal prostate, bladder, skeletal muscle and colon. Increased expression of 10-H10 was seen in prostate tumor and normal prostate, bladder, lung,

30 colon, brain and large intestine. Increased expression of 9-B1 was seen in prostate tumor, breast tumor, and normal prostate, salivary gland, large intestine and skin, with increased expression of 11-C8 being seen in prostate tumor, and normal prostate and large intestine.

An additional cDNA fragment derived from the PCR-based normal prostate subtraction, described above, was found to be prostate specific by both micro-array technology and RT-PCR. The determined cDNA sequence of this clone (referred to as 9-A11) is provided in SEQ ID NO: 226. Comparison of this sequence with those in the public databases revealed 99% identity
5 to the known gene HOXB13.

Further studies led to the isolation of the clones 8-C6 and 8-H7. The determined cDNA sequences for these clones are provided in SEQ ID NO: 227 and 228, respectively. These sequences were found to show some homology to previously isolated ESTs.

PCR and hybridization-based methodologies were employed to obtain longer cDNA
10 sequences for clone P20 (also referred to as P703P), yielding three additional cDNA fragments that progressively extend the 5' end of the gene. These fragments, referred to as P703PDE5, P703P6.26, and P703PX-23 (SEQ ID NO: 326, 328 and 330, with the predicted corresponding amino acid sequences being provided in SEQ ID NO: 327, 329 and 331, respectively) contain additional 5' sequence. P703PDE5 was recovered by screening of a cDNA library (#141-26) with a portion of
15 P703P as a probe. P703P6.26 was recovered from a mixture of three prostate tumor cDNAs and P703PX_23 was recovered from cDNA library (#438-48). Together, the additional sequences include all of the putative mature serine protease along with part of the putative signal sequence. The putative full-length cDNA sequence for P703P is provided in SEQ ID NO: 524, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 525.

20   Further studies using a PCR-based subtraction library of a prostate tumor pool subtracted against a pool of normal tissues (referred to as JP: PCR subtraction) resulted in the isolation of thirteen additional clones, seven of which did not share any significant homology to known GenBank sequences. The determined cDNA sequences for these seven clones (P711P, P712P, novel 23, P774P, P775P, P710P and P768P) are provided in SEQ ID NO: 307-311, 313 and
25 315, respectively. The remaining six clones (SEQ ID NO: 316 and 321-325) were shown to share some homology to known genes. By microarray analysis, all thirteen clones showed three or more fold over-expression in prostate tissues, including prostate tumors, BPH and normal prostate as compared to normal non-prostate tissues. Clones P711P, P712P, novel 23 and P768P showed over-expression in most prostate tumors and BPH tissues tested (n=29), and in the majority of normal
30 prostate tissues (n=4), but background to low expression levels in all normal tissues. Clones P774P, P775P and P710P showed comparatively lower expression and expression in fewer prostate tumors and BPH samples, with negative to low expression in normal prostate.

67

The full-length cDNA for P711P was obtained by employing the partial sequence of SEQ ID NO: 307 to screen a prostate cDNA library. Specifically, a directionally cloned prostate cDNA library was prepared using standard techniques. One million colonies of this library were plated onto LB/Amp plates. Nylon membrane filters were used to lift these colonies, and the cDNAs which were picked up by these filters were denatured and cross-linked to the filters by UV light. The P711P cDNA fragment of SEQ ID NO: 307 was radio-labeled and used to hybridize with these filters. Positive clones were selected, and cDNAs were prepared and sequenced using an automatic Perkin Elmer/Applied Biosystems sequencer. The determined full-length sequence of P711P is provided in SEQ ID NO: 382, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 383.

Using PCR and hybridization-based methodologies, additional cDNA sequence information was derived for two clones described above, 11-C9 and 9-F3, herein after referred to as P707P and P714P, respectively (SEQ ID NO: 333 and 334). After comparison with the most recent GenBank, P707P was found to be a splice variant of the known gene HoxB13. In contrast, no significant homologies to P714P were found.

Clones 8-B3, P89, P98, P130 and P201 (as disclosed in U.S. Patent Application No. 09/020,956, filed February 9, 1998) were found to be contained within one contiguous sequence, referred to as P705P (SEQ ID NO: 335, with the predicted amino acid sequence provided in SEQ ID NO: 336), which was determined to be a splice variant of the known gene NKX 3.1.

Further studies on P775P resulted in the isolation of four additional sequences (SEQ ID NO: 473-476) which are all splice variants of the P775P gene. The sequence of SEQ ID NO: 474 was found to contain two open reading frames (ORFs). The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 477 and 478. The cDNA sequence of SEQ ID NO: 475 was found to contain an ORF which encodes the amino acid sequence of SEQ ID NO: 479. The cDNA sequence of SEQ ID NO: 473 was found to contain four ORFs. The predicted amino acid sequences encoded by these ORFs are provided in SEQ ID NO: 480-483.

Subsequent studies led to the identification of a genomic region on chromosome 22q11.2, known as the Cat Eye Syndrome region, that contains the five prostate genes P704P, P712P, P774P, P775P and B305D. The relative location of each of these five genes within the genomic region is shown in Fig. 10. This region may therefore be associated with malignant tumors, and other potential tumor genes may be contained within this region. These studies also led

to the identification of a potential open reading frame (ORF) for P775P (provided in SEQ ID NO: 533), which encodes the amino acid sequence of SEQ ID NO: 534.

EXAMPLE 4

5

SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems 430A peptide synthesizer using FMOC chemistry with HPTU (O-Benzotriazole-N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence may be attached to 10 the amino terminus of the peptide to provide a method of conjugation, binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from the solid support may be carried out using the following cleavage mixture: trifluoroacetic acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be dissolved in 15 water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing 0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following lyophilization of the pure fractions, the peptides may be characterized using electrospray or other types of mass spectrometry and by amino acid analysis.

20

EXAMPLE 5

FURTHER ISOLATION AND CHARACTERIZATION OF PROSTATE-SPECIFIC POLYPEPTIDES BY PCR-BASED SUBTRACTION

25

A cDNA library generated from prostate primary tumor mRNA as described above was subtracted with cDNA from normal prostate. The subtraction was performed using a PCR-based protocol (Clontech), which was modified to generate larger fragments. Within this protocol, tester and driver double stranded cDNA were separately digested with five restriction enzymes that 30 recognize six-nucleotide restriction sites (MluI, MscI, PvuII, SalI and StuI). This digestion resulted in an average cDNA size of 600 bp, rather than the average size of 300 bp that results from digestion with RsaI according to the Clontech protocol. This modification did not affect the

subtraction efficiency. Two tester populations were then created with different adapters, and the driver library remained without adapters.

5 The tester and driver libraries were then hybridized using excess driver cDNA. In the first hybridization step, driver was separately hybridized with each of the two tester cDNA populations. This resulted in populations of (a) unhybridized tester cDNAs, (b) tester cDNAs hybridized to other tester cDNAs, (c) tester cDNAs hybridized to driver cDNAs and (d) unhybridized driver cDNAs. The two separate hybridization reactions were then combined, and rehybridized in the presence of additional denatured driver cDNA. Following this second hybridization, in addition to populations (a) through (d), a fifth population (e) was generated in

10 which tester cDNA with one adapter hybridized to tester cDNA with the second adapter. Accordingly, the second hybridization step resulted in enrichment of differentially expressed sequences which could be used as templates for PCR amplification with adaptor-specific primers.

The ends were then filled in, and PCR amplification was performed using adaptor-specific primers. Only population (e), which contained tester cDNA that did not hybridize to driver

15 cDNA, was amplified exponentially. A second PCR amplification step was then performed, to reduce background and further enrich differentially expressed sequences.

This PCR-based subtraction technique normalizes differentially expressed cDNAs so that rare transcripts that are overexpressed in prostate tumor tissue may be recoverable. Such transcripts would be difficult to recover by traditional subtraction methods.

20 In addition to genes known to be overexpressed in prostate tumor, seventy-seven further clones were identified. Sequences of these partial cDNAs are provided in SEQ ID NO: 29 to 305. Most of these clones had no significant homology to database sequences. Exceptions were JPTPN23 (SEQ ID NO: 231; similarity to pig valosin-containing protein), JPTPN30 (SEQ ID NO: 234; similarity to rat mRNA for proteasome subunit), JPTPN45 (SEQ ID NO: 243; similarity to rat

25 *norvegicus* cytosolic NADP-dependent isocitrate dehydrogenase), JPTPN46 (SEQ ID NO: 244; similarity to human subclone H8 4 d4 DNA sequence), JP1D6 (SEQ ID NO: 265; similarity to *G. gallus* dynein light chain-A), JP8D6 (SEQ ID NO: 288; similarity to human BAC clone RG016J04), JP8F5 (SEQ ID NO: 289; similarity to human subclone H8 3 b5 DNA sequence), and JP8E9 (SEQ ID NO: 299; similarity to human Alu sequence).

30 Additional studies using the PCR-based subtraction library consisting of a prostate tumor pool subtracted against a normal prostate pool (referred to as PT-PN PCR subtraction) yielded three additional clones. Comparison of the cDNA sequences of these clones with the most

recent release of GenBank revealed no significant homologies to the two clones referred to as P715P and P767P (SEQ ID NO: 312 and 314). The remaining clone was found to show some homology to the known gene KIAA0056 (SEQ ID NO: 318). Using microarray analysis to measure mRNA expression levels in various tissues, all three clones were found to be over-expressed in

5   prostate tumors and BPH tissues. Specifically, clone P715P was over-expressed in most prostate tumors and BPH tissues by a factor of three or greater, with elevated expression seen in the majority of normal prostate samples and in fetal tissue, but negative to low expression in all other normal tissues. Clone P767P was over-expressed in several prostate tumors and BPH tissues, with moderate expression levels in half of the normal prostate samples, and background to low

10   expression in all other normal tissues tested.

Further analysis, by microarray as described above, of the PT-PN PCR subtraction library and of a DNA subtraction library containing cDNA from prostate tumor subtracted with a pool of normal tissue cDNAs, led to the isolation of 27 additional clones (SEQ ID NO: 340-365 and 381) which were determined to be over-expressed in prostate tumor. The clones of SEQ ID NO:

15   341, 342, 345, 347, 348, 349, 351, 355-359, 361, 362 and 364 were also found to be expressed in normal prostate. Expression of all 26 clones in a variety of normal tissues was found to be low or undetectable, with the exception of P544S (SEQ ID NO: 356) which was found to be expressed in small intestine. Of the 26 clones, 10 (SEQ ID NO: 340-349) were found to show some homology to previously identified sequences. No significant homologies were found to the clones of SEQ ID

20   NO: 350, 351 and 353-365.

Further studies on the clone of SEQ ID NO: 352 (referred to as P790P) led to the isolation of the full-length cDNA sequence of SEQ ID NO: 526. The corresponding predicted amino acid is provided in SEQ ID NO: 527. Data from two quantitative PCR experiments indicated that P790P is over-expressed in 11/15 tested prostate tumor samples and is expressed at low levels

25   in spinal cord, with no expression being seen in all other normal samples tested. Data from further PCR experiments and microarray experiments showed over-expression in normal prostate and prostate tumor with little or no expression in other tissues tested. P790P was subsequently found to show significant homology to a previously identified G-protein coupled prostate tissue receptor.

71

EXAMPLE 6

PEPTIDE PRIMING OF MICE AND PROPAGATION OF CTL LINES

5   6.1. This Example illustrates the preparation of a CTL cell line specific for cells expressing the P502S gene.

Mice expressing the transgene for human HLA A2Kb (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with P2S#12 peptide (VLGWVAEL; SEQ ID NO: 306), which is derived from the P502S gene (also referred to herein as J1-17, SEQ ID

10   NO: 8), as described by Theobald et al., *Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995 with the following modifications. Mice were immunized with 100µg of P2S#12 and 120µg of an I-A^b binding peptide derived from hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and using a nylon mesh single cell suspensions prepared. Cells were then resuspended at 6×10^6 cells/ml in complete media (RPMI-1640; Gibco

15   BRL, Gaithersburg, MD) containing 10% FCS, 2mM Glutamine (Gibco BRL), sodium pyruvate (Gibco BRL), non-essential amino acids (Gibco BRL), 2×10^{-5} M 2-mercaptoethanol, 50U/ml penicillin and streptomycin, and cultured in the presence of irradiated (3000 rads) P2S#12-pulsed (5mg/ml P2S#12 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later, cells ($5 \times$

20   10^5/ml) were restimulated with 2.5×10^6/ml peptide pulsed irradiated (20,000 rads) EL4A2Kb cells (Sherman et al, *Science 258*:815-818, 1992) and 3×10^6/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20U/ml IL-2. Cells continued to be restimulated on a weekly basis as described, in preparation for cloning the line.

P2S#12 line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb

25   tumor cells (1×10^4 cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5×10^5 cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, clones that were growing were isolated and maintained in culture. Several of these clones demonstrated significantly higher reactivity (lysis) against human fibroblasts (HLA A2Kb expressing) transduced with P502S than against control fibroblasts. An example is presented in

30   Figure 1.

This data indicates that P2S #12 represents a naturally processed epitope of the P502S protein that is expressed in the context of the human HLA A2Kb molecule.

6.2. This Example illustrates the preparation of murine CTL lines and CTL clones specific for cells expressing the P501S gene.

This series of experiments were performed similarly to that described above. Mice

5 were immunized with the P1S#10 peptide (SEQ ID NO: 337), which is derived from the P501S gene (also referred to herein as L1-12, SEQ ID NO: 110). The P1S#10 peptide was derived by analysis of the predicted polypeptide sequence for P501S for potential HLA-A2 binding sequences as defined by published HLA-A2 binding motifs (Parker, KC, *et al*, *J. Immunol.*, 152:163, 1994). P1S#10 peptide was synthesized as described in Example 4, and empirically tested for HLA-A2

10 binding using a T cell based competition assay. Predicted A2 binding peptides were tested for their ability to compete HLA-A2 specific peptide presentation to an HLA-A2 restricted CTL clone (D150M58), which is specific for the HLA-A2 binding influenza matrix peptide fluM58. D150M58 CTL secretes TNF in response to self-presentation of peptide fluM58. In the competition assay, test peptides at 100-200 µg/ml were added to cultures of D150M58 CTL in order to bind HLA-A2 on

15 the CTL. After thirty minutes, CTL cultured with test peptides, or control peptides, were tested for their antigen dose response to the fluM58 peptide in a standard TNF bioassay. As shown in Figure 3, peptide P1S#10 competes HLA-A2 restricted presentation of fluM58, demonstrating that peptide P1S#10 binds HLA-A2.

Mice expressing the transgene for human HLA A2Kb were immunized as described

20 by Theobald et al. (*Proc. Natl. Acad. Sci. USA 92*:11993-11997, 1995) with the following modifications. Mice were immunized with 62.5µg of P1S #10 and 120µg of an I-A^b binding peptide derived from Hepatitis B Virus protein emulsified in incomplete Freund's adjuvant. Three weeks later these mice were sacrificed and single cell suspensions prepared using a nylon mesh. Cells were then resuspended at 6 x 10^6 cells/ml in complete media (as described above) and cultured

25 in the presence of irradiated (3000 rads) P1S#10-pulsed (2µg/ml P1S#10 and 10mg/ml β2-microglobulin) LPS blasts (A2 transgenic spleens cells cultured in the presence of 7µg/ml dextran sulfate and 25µg/ml LPS for 3 days). Six days later cells (5 x 10^5/ml) were restimulated with 2.5 x 10^6/ml peptide-pulsed irradiated (20,000 rads) EL4A2Kb cells, as described above, and 3 x 10^6/ml A2 transgenic spleen feeder cells. Cells were cultured in the presence of 20 U/ml IL-2. Cells were

30 restimulated on a weekly basis in preparation for cloning. After three rounds of *in vitro* stimulations, one line was generated that recognized P1S#10-pulsed Jurkat A2Kb targets and P501S-transduced Jurkat targets as shown in Figure 4.

A P1S#10-specific CTL line was cloned by limiting dilution analysis with peptide pulsed EL4 A2Kb tumor cells (1 x 10⁴ cells/ well) as stimulators and A2 transgenic spleen cells as feeders (5 x 10⁵ cells/ well) grown in the presence of 30U/ml IL-2. On day 14, cells were restimulated as before. On day 21, viable clones were isolated and maintained in culture. As shown in Figure 5, five of these clones demonstrated specific cytolytic reactivity against P501S-transduced Jurkat A2Kb targets. This data indicates that P1S#10 represents a naturally processed epitope of the P501S protein that is expressed in the context of the human HLA-A2.1 molecule.

EXAMPLE 7

PRIMING OF CTL *IN VIVO* USING NAKED DNA IMMUNIZATION
WITH A PROSTATE ANTIGEN

The prostate-specific antigen L1-12, as described above, is also referred to as P501S. HLA A2Kb Tg mice (provided by Dr L. Sherman, The Scripps Research Institute, La Jolla, CA) were immunized with 100 μg P501S in the vector VR1012 either intramuscularly or intradermally. The mice were immunized three times, with a two week interval between immunizations. Two weeks after the last immunization, immune spleen cells were cultured with Jurkat A2Kb-P501S transduced stimulator cells. CTL lines were stimulated weekly. After two weeks of *in vitro* stimulation, CTL activity was assessed against P501S transduced targets. Two out of 8 mice developed strong anti-P501S CTL responses. These results demonstrate that P501S contains at least one naturally processed HLA-A2-restricted CTL epitope.

EXAMPLE 8

ABILITY OF HUMAN T CELLS TO RECOGNIZE PROSTATE-SPECIFIC POLYPEPTIDES

This Example illustrates the ability of T cells specific for a prostate tumor polypeptide to recognize human tumor.

Human CD8⁺ T cells were primed *in vitro* to the P2S-12 peptide (SEQ ID NO: 306) derived from P502S (also referred to as J1-17) using dendritic cells according to the protocol of Van Tsai et al. (*Critical Reviews in Immunology 18*:65-75, 1998). The resulting CD8⁺ T cell microcultures were tested for their ability to recognize the P2S-12 peptide presented by autologous fibroblasts or fibroblasts which were transduced to express the P502S gene in a γ-interferon

ELISPOT assay (*see* Lalvani et al., *J. Exp. Med.* 186:859-865, 1997). Briefly, titrating numbers of T cells were assayed in duplicate on 10^4 fibroblasts in the presence of 3 μg/ml human β₂-microglobulin and 1 μg/ml P2S-12 peptide or control E75 peptide. In addition, T cells were simultaneously assayed on autologous fibroblasts transduced with the P502S gene or as a control,

5   fibroblasts transduced with HER-2/*neu*. Prior to the assay, the fibroblasts were treated with 10 ng/ml γ-interferon for 48 hours to upregulate class I MHC expression. One of the microcultures (#5) demonstrated strong recognition of both peptide pulsed fibroblasts as well as transduced fibroblasts in a γ-interferon ELISPOT assay. Figure 2A demonstrates that there was a strong increase in the number of γ-interferon spots with increasing numbers of T cells on fibroblasts pulsed

10   with the P2S-12 peptide (solid bars) but not with the control E75 peptide (open bars). This shows the ability of these T cells to specifically recognize the P2S-12 peptide. As shown in Figure 2B, this microculture also demonstrated an increase in the number of γ-interferon spots with increasing numbers of T cells on fibroblasts transduced to express the P502S gene but not the HER-2/*neu* gene. These results provide additional confirmatory evidence that the P2S-12 peptide is a naturally

15   processed epitope of the P502S protein. Furthermore, this also demonstrates that there exists in the human T cell repertoire, high affinity T cells which are capable of recognizing this epitope. These T cells should also be capable of recognizing human tumors which express the P502S gene.

20   EXAMPLE 9

ELICITATION OF PROSTATE ANTIGEN-SPECIFIC CTL RESPONSES
IN HUMAN BLOOD

         This Example illustrates the ability of a prostate-specific antigen to elicit a CTL

25   response in blood of normal humans.

         Autologous dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal donors by growth for five days in RPMI medium containing 10% human serum, 50 ng/ml GMCSF and 30 ng/ml IL-4. Following culture, DC were infected overnight with recombinant P501S-expressing vaccinia virus at an M.O.I. of 5 and matured for 8 hours by the

30   addition of 2 micrograms/ml CD40 ligand. Virus was inactivated by UV irradiation, CD8⁺ cells were isolated by positive selection using magnetic beads, and priming cultures were initiated in 24-well plates. Following five stimulation cycles using autologous fibroblasts retrovirally transduced

to express P501S and CD80, CD8+ lines were identified that specifically produced interferon-gamma when stimulated with autologous P501S-transduced fibroblasts. The P501S-specific activity of cell line 3A-1 could be maintained following additional stimulation cycles on autologous B-LCL transduced with P501S. Line 3A-1 was shown to specifically recognize autologous B-LCL

5   transduced to express P501S, but not EGFP-transduced autologous B-LCL, as measured by cytotoxicity assays (^{51}Cr release) and interferon-gamma production (Interferon-gamma Elispot; *see* above and Lalvani et al., *J. Exp. Med. 186*:859-865, 1997). The results of these assays are presented in Figures 6A and 6B.

10   EXAMPLE 10

IDENTIFICATION OF A NATURALLY PROCESSED CTL EPITOPE CONTAINED WITHIN A
                        PROSTATE-SPECIFIC ANTIGEN

        The 9-mer peptide p5 (SEQ ID NO: 338) was derived from the P703P antigen (also

15 referred to as P20). The p5 peptide is immunogenic in human HLA-A2 donors and is a naturally processed epitope. Antigen specific human CD8+ T cells can be primed following repeated *in vitro* stimulations with monocytes pulsed with p5 peptide. These CTL specifically recognize p5-pulsed and P703P-transduced target cells in both ELISPOT (as described above) and chromium release assays. Additionally, immunization of HLA-A2Kb transgenic mice with p5 leads to the generation

20 of CTL lines which recognize a variety of HLA-A2Kb or HLA-A2 transduced target cells expressing P703P.

        Initial studies demonstrating that p5 is a naturally processed epitope were done using HLA-A2Kb transgenic mice. HLA-A2Kb transgenic mice were immunized subcutaneously in the footpad with 100 μg of p5 peptide together with 140 μg of hepatitis B virus core peptide (a Th

25 peptide) in Freund's incomplete adjuvant. Three weeks post immunization, spleen cells from immunized mice were stimulated *in vitro* with peptide-pulsed LPS blasts. CTL activity was assessed by chromium release assay five days after primary *in vitro* stimulation. Retrovirally transduced cells expressing the control antigen P703P and HLA-A2Kb were used as targets. CTL lines that specifically recognized both p5-pulsed targets as well as P703P-expressing targets were

30 identified.

        Human *in vitro* priming experiments demonstrated that the p5 peptide is immunogenic in humans. Dendritic cells (DC) were differentiated from monocyte cultures derived

from PBMC of normal human donors by culturing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, the DC were pulsed with 1 ug/ml p5 peptide and cultured with CD8+ T cell enriched PBMC. CTL lines were restimulated on a weekly basis with p5-pulsed monocytes. Five to six weeks after initiation of

5   the CTL cultures, CTL recognition of p5-pulsed target cells was demonstrated. CTL were additionally shown to recognize human cells transduced to express P703P, demonstrating that p5 is a naturally processed epitope.

EXAMPLE 11

10   EXPRESSION OF A BREAST TUMOR-DERIVED ANTIGEN

IN PROSTATE

Isolation of the antigen B305D from breast tumor by differential display is described in US Patent Application No. 08/700,014, filed August 20, 1996. Several different splice forms of this antigen were isolated. The determined cDNA sequences for these splice forms are provided in

15   SEQ ID NO: 366-375, with the predicted amino acid sequences corresponding to the sequences of SEQ ID NO: 292, 298 and 301-303 being provided in SEQ ID NO: 299-306, respectively. In further studies, a splice variant of the cDNA sequence of SEQ ID NO: 366 was isolated which was found to contain an additional guanine residue at position 884 (SEQ ID NO: 530), leading to a frameshift in the open reading frame. The determined DNA sequence of this ORF is provided in

20   SEQ ID NO: 531. This frameshift generates a protein sequence (provided in SEQ ID NO: 532) of 293 amino acids that contains the C-terminal domain common to the other isoforms of B305D but that differs in the N-terminal region.

The expression levels of B305D in a variety of tumor and normal tissues were examined by real time PCR and by Northern analysis. The results indicated that B305D is highly

25   expressed in breast tumor, prostate tumor, normal prostate and normal testes, with expression being low or undetectable in all other tissues examined (colon tumor, lung tumor, ovary tumor, and normal bone marrow, colon, kidney, liver, lung, ovary, skin, small intestine, stomach).

EXAMPLE 12

30   GENERATION OF HUMAN CTL *IN VITRO* USING WHOLE GENE PRIMING AND

STIMULATION TECHNIQUES WITH PROSTATE-SPECIFIC ANTIGEN

Using *in vitro* whole-gene priming with P501S-vaccinia infected DC (see, for example, Yee et al, *The Journal of Immunology*, 157(9):4079-86, 1996), human CTL lines were derived that specifically recognize autologous fibroblasts transduced with P501S (also known as L1-12), as determined by interferon-γ ELISPOT analysis as described above. Using a panel of

5   HLA-mismatched B-LCL lines transduced with P501S, these CTL lines were shown to be likely restricted to HLAB class I allele. Specifically, dendritic cells (DC) were differentiated from monocyte cultures derived from PBMC of normal human donors by growing for five days in RPMI medium containing 10% human serum, 50 ng/ml human GM-CSF and 30 ng/ml human IL-4. Following culture, DC were infected overnight with recombinant P501S vaccinia virus at a

10 multiplicity of infection (M.O.I) of five, and matured overnight by the addition of 3 μg/ml CD40 ligand. Virus was inactivated by UV irradiation. CD8+ T cells were isolated using a magnetic bead system, and priming cultures were initiated using standard culture techniques. Cultures were restimulated every 7-10 days using autologous primary fibroblasts retrovirally transduced with P501S and CD80. Following four stimulation cycles, CD8+ T cell lines were identified that

15 specifically produced interferon-γ when stimulated with P501S and CD80-transduced autologous fibroblasts. A panel of HLA-mismatched B-LCL lines transduced with P501S were generated to define the restriction allele of the response. By measuring interferon-γ in an ELISPOT assay, the P501S specific response was shown to be likely restricted by HLA B alleles. These results demonstrate that a CD8+ CTL response to P501S can be elicited.

20   To identify the epitope(s) recognized, cDNA encoding P501S was fragmented by various restriction digests, and sub-cloned into the retroviral expression vector pBIB-KS. Retroviral supernatants were generated by transfection of the helper packaging line Phoenix-Ampho. Supernatants were then used to transduce Jurkat/A2Kb cells for CTL screening. CTL were screened in IFN-gamma ELISPOT assays against these A2Kb targets transduced with the "library" of P501S

25 fragments. Initial positive fragments P501S/H3 and P501S/F2 were sequenced and found to encode amino acids 106-553 and amino acids 136-547, respectively, of SEQ ID NO: 113. A truncation of H3 was made to encode amino acid residues 106-351 of SEQ ID NO: 113, which was unable to stimulate the CTL, thus localizing the epitope to amino acid residues 351-547. Additional fragments encoding amino acids 1-472 (Fragment A) and amino acids 1-351 (Fragment B) were

30 also constructed. Fragment A but not Fragment B stimulated the CTL thus localizing the epitope to amino acid residues 351-472. Overlapping 20-mer and 18-mer peptides representing this region were tested by pulsing Jurkat/A2Kb cells versus CTL in an IFN-gamma assay. Only peptides

P501S-369(20) and P501S-369(18) stimulated the CTL. Nine-mer and 10-mer peptides representing this region were synthesized and similarly tested. Peptide P501S-370 (SEQ ID NO: 539) was the minimal 9-mer giving a strong response. Peptide P501S-376 (SEQ ID NO: 540) also gave a weak response, suggesting that it might represent a cross-reactive epitope.

5   In subsequent studies, the ability of primary human B cells transduced with P501S to prime MHC class I-restricted, P501S-specific, autologous CD8 T cells was examined. Primary B cells were derived from PBMC of a homozygous HLA-A2 donor by culture in CD40 ligand and IL-4, transduced at high frequency with recombinant P501S in the vector pBIB, and selected with blastocidin-S. For *in vitro* priming, purified CD8+ T cells were cultured with autologous CD40 ligand + IL-4 derived, P501S-transduced B cells in a 96-well microculture format. These CTL microcultures were re-stimulated with P501S-transduced B cells and then assayed for specificity. Following this initial screen, microcultures with significant signal above background were cloned on autologous EBV-transformed B cells (BLCL), also transduced with P501S. Using IFN-gamma ELISPOT for detection, several of these CD8 T cell clones were found to be specific for P501S, as demonstrated by reactivity to BLCL/P501S but not BLCL transduced with control antigen. It was further demonstrated that the anti-P501S CD8 T cell specificity is HLA-A2-restricted. First, antibody blocking experiments with anti-HLA-A,B,C monoclonal antibody (W6.32), anti-HLA-B,C monoclonal antibody (B1.23.2) and a control monoclonal antibody showed that only the anti-HLA-A,B,C antibody blocked recognition of P501S-expressing autologous BLCL. Secondly, the anti-P501S CTL also recognized an HLA-A2 matched, heterologous BLCL transduced with P501S, but not the corresponding EGFP transduced control BLCL.

EXAMPLE 13

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

BY MICROARRAY ANALYSIS

25

           This Example describes the isolation of certain prostate-specific polypeptides from a prostate tumor cDNA library.

           A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 372 clones were identified, and 319 were successfully sequenced. Table I presents a summary of these clones, which are shown in SEQ ID NOs:385-400. Of these sequences

SEQ ID NOs:386, 389, 390 and 392 correspond to novel genes, and SEQ ID NOs: 393 and 396 correspond to previously identified sequences. The others (SEQ ID NOs:385, 387, 388, 391, 394, 395 and 397-400) correspond to known sequences, as shown in Table I.

5

Table I

Summary of Prostate Tumor Antigens

Known Genes	Previously Identified Genes	Novel Genes
T-cell gamma chain	P504S	23379 (SEQ ID NO:389)
Kallikrein	P1000C	23399 (SEQ ID NO:392)
Vector	P501S	23320 (SEQ ID NO:386)
CGI-82 protein mRNA (23319; SEQ ID NO:385)	P503S	23381 (SEQ ID NO:390)
PSA	P510S	
Ald. 6 Dehyd.	P784P	
L-iditol-2 dehydrogenase (23376; SEQ ID NO:388)	P502S	
Ets transcription factor PDEF (22672; SEQ ID NO:398)	P706P	
hTGR (22678; SEQ ID NO:399)	19142.2, bangur.seq (22621; SEQ ID NO:396)	
KIAA0295(22685; SEQ ID NO:400)	5566.1 Wang (23404; SEQ ID NO:393)	
Prostatic Acid Phosphatase(22655; SEQ ID NO:397)	P712P	
transglutaminase (22611; SEQ ID NO:395)	P778P	
HDLBP (23508; SEQ ID NO:394)		
CGI-69 Protein(23367; SEQ ID NO:387)		
KIAA0122(23383; SEQ ID NO:391)		
TEEG		

CGI-82 showed 4.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 43% of prostate tumors, 25% normal prostate, not detected in other normal tissues tested. L-iditol-2 dehydrogenase showed 4.94 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 90% of

5   prostate tumors, 100% of normal prostate, and not detected in other normal tissues tested. Ets transcription factor PDEF showed 5.55 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% prostate tumors, 25% normal prostate and not detected in other normal tissues tested. hTGR1 showed 9.11 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 63% of prostate tumors and is

10   not detected in normal tissues tested including normal prostate. KIAA0295 showed 5.59 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 47% of prostate tumors, low to undetectable in normal tissues tested including normal prostate tissues. Prostatic acid phosphatase showed 9.14 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 67% of prostate tumors, 50% of

15   normal prostate, and not detected in other normal tissues tested. Transglutaminase showed 14.84 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 30% of prostate tumors, 50% of normal prostate, and is not detected in other normal tissues tested. High density lipoprotein binding protein (HDLBP) showed 28.06 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in

20   97% of prostate tumors, 75% of normal prostate, and is undetectable in all other normal tissues tested. CGI-69 showed 3.56 fold over-expression in prostate tissues as compared to other normal tissues tested. It is a low abundant gene, detected in more than 90% of prostate tumors, and in 75% normal prostate tissues. The expression of this gene in normal tissues was very low. KIAA0122 showed 4.24 fold over-expression in prostate tissues as compared to other normal tissues tested. It

25   was over-expressed in 57% of prostate tumors, it was undetectable in all normal tissues tested including normal prostate tissues. 19142.2 bangur showed 23.25 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 97% of prostate tumors and 100% of normal prostate. It was undetectable in other normal tissues tested. 5566.1 Wang showed 3.31 fold over-expression in prostate tissues as compared to other normal tissues tested. It

30   was over-expressed in 97% of prostate tumors, 75% normal prostate and was also over-expressed in normal bone marrow, pancreas, and activated PBMC. Novel clone 23379 showed 4.86 fold over-expression in prostate tissues as compared to other normal tissues tested. It was detectable in 97%

of prostate tumors and 75% normal prostate and is undetectable in all other normal tissues tested. Novel clone 23399 showed 4.09 fold over-expression in prostate tissues as compared to other normal tissues tested. It was over-expressed in 27% of prostate tumors and was undetectable in all normal tissues tested including normal prostate tissues. Novel clone 23320 showed 3.15 fold over-

5   expression in prostate tissues as compared to other normal tissues tested. It was detectable in all prostate tumors and 50% of normal prostate tissues. It was also expressed in normal colon and trachea. Other normal tissues do not express this gene at high level.

10   EXAMPLE 14

IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS

BY ELECTRONIC SUBTRACTION

        This Example describes the use of an electronic subtraction technique to identify
15   prostate-specific antigens.

        Potential prostate-specific genes present in the GenBank human EST database were identified by electronic subtraction (similar to that described by Vasmatizis et al., *Proc. Natl. Acad. Sci. USA* 95:300-304, 1998). The sequences of EST clones (43,482) derived from various prostate libraries were obtained from the GenBank public human EST database. Each prostate EST

20   sequence was used as a query sequence in a BLASTN (National Center for Biotechnology Information) search against the human EST database. All matches considered identical (length of matching sequence >100 base pairs, density of identical matches over this region > 70%) were grouped (aligned) together in a cluster. Clusters containing more than 200 ESTs were discarded since they probably represented repetitive elements or highly expressed genes such as those for

25   ribosomal proteins. If two or more clusters shared common ESTs, those clusters were grouped together into a "supercluster," resulting in 4,345 prostate superclusters.

        Records for the 479 human cDNA libraries represented in the GenBank release were downloaded to create a database of these cDNA library records. These 479 cDNA libraries were grouped into three groups: Plus (normal prostate and prostate tumor libraries, and breast cell line

30   libraries, in which expression was desired), Minus (libraries from other normal adult tissues, in which expression was not desirable), and Other (libraries from fetal tissue, infant tissue, tissues found only in women, non-prostate tumors and cell lines other than prostate cell lines, in which

expression was considered to be irrelevant). A summary of these library groups is presented in Table II.

<p style="text-align:center">Table II</p>

<p style="text-align:center">Prostate cDNA Libraries and ESTs</p>

Library	# of Libraries	# of ESTs
Plus	25	43,482
Normal	11	18,875
Tumor	11	21,769
Cell lines	3	2,838
Minus	166	
Other	287	

Each supercluster was analyzed in terms of the ESTs within the supercluster. The tissue source of each EST clone was noted and used to classify the superclusters into four groups: Type 1- EST clones found in the Plus group libraries only; no expression detected in Minus or Other group libraries; Type 2- EST clones derived from the Plus and Other group libraries only; no expression detected in the Minus group; Type 3- EST clones derived from the Plus, Minus and Other group libraries, but the number of ESTs derived from the Plus group is higher than in either the Minus or Other groups; and Type 4- EST clones derived from Plus, Minus and Other group libraries, but the number derived from the Plus group is higher than the number derived from the Minus group. This analysis identified 4,345 breast clusters (see Table III). From these clusters, 3,172 EST clones were ordered from Research Genetics, Inc., and were received as frozen glycerol stocks in 96-well plates.

Table III

Prostate Cluster Summary

Type	# of Superclusters	# of ESTs Ordered
1	688	677
2	2899	2484
3	85	11
4	673	0
Total	4345	3172

The EST clone inserts were PCR-amplified using amino-linked PCR primers for Synteni microarray analysis. When more than one PCR product was obtained for a particular clone, that PCR product was not used for expression analysis. In total, 2,528 clones from the electronic subtraction method were analyzed by microarray analysis to identify electronic subtraction breast clones that had high levels of tumor vs. normal tissue mRNA. Such screens were performed using a Synteni (Palo Alto, CA) microarray, according to the manufacturer's instructions (and essentially as described by Schena et al., *Proc. Natl. Acad. Sci. USA* 93:10614-10619, 1996 and Heller et al., *Proc. Natl. Acad. Sci. USA* 94:2150-2155, 1997). Within these analyses, the clones were arrayed on the chip, which was then probed with fluorescent probes generated from normal and tumor prostate cDNA, as well as various other normal tissues. The slides were scanned and the fluorescence intensity was measured.

Clones with an expression ratio greater than 3 (*i.e.*, the level in prostate tumor and normal prostate mRNA was at least three times the level in other normal tissue mRNA) were identified as prostate tumor-specific sequences (Table IV). The sequences of these clones are provided in SEQ ID NO: 401-453, with certain novel sequences shown in SEQ ID NO: 407, 413, 416-419, 422, 426, 427 and 450.

Table IV

Prostate-tumor Specific Clones

SEQ ID NO.	Sequence Designation	Comments
401	22545	previously identified P1000C
402	22547	previously identified P704P
403	22548	known
404	22550	known
405	22551	PSA
406	22552	prostate secretory protein 94
407	22553	novel
408	22558	previously identified P509S
409	22562	glandular kallikrein
410	22565	previously identified P1000C
411	22567	PAP
412	22568	B1006C (breast tumor antigen)
413	22570	novel
414	22571	PSA
415	22572	previously identified P706P
416	22573	novel
417	22574	novel
418	22575	novel
419	22580	novel
420	22581	PAP
421	22582	prostatic secretory protein 94
422	22583	novel
423	22584	prostatic secretory protein 94
424	22585	prostatic secretory protein 94
425	22586	known
426	22587	novel
427	22588	novel
428	22589	PAP
429	22590	known
430	22591	PSA
431	22592	known
432	22593	Previously identified P777P
433	22594	T cell receptor gamma chain
434	22595	Previously identified P705P
435	22596	Previously identified P707P
436	22847	PAP
437	22848	known
438	22849	prostatic secretory protein 57
439	22851	PAP

440	22852	PAP
441	22853	PAP
442	22854	previously identified P509S
443	22855	previously identified P705P
444	22856	previously identified P774P
445	22857	PSA
446	23601	previously identified P777P
447	23602	PSA
448	23605	PSA
449	23606	PSA
450	23612	novel
451	23614	PSA
452	23618	previously identified P1000C
453	23622	previously identified P705P

EXAMPLE 15

FURTHER IDENTIFICATION OF PROSTATE-SPECIFIC ANTIGENS BY MICROARRAY ANALYSIS

This Example describes the isolation of additional prostate-specific polypeptides from a prostate tumor cDNA library.

A human prostate tumor cDNA expression library as described above was screened using microarray analysis to identify clones that display at least a three fold over-expression in prostate tumor and/or normal prostate tissue, as compared to non-prostate normal tissues (not including testis). 142 clones were identified and sequenced. Certain of these clones are shown in SEQ ID NO: 454-467. Of these sequences, SEQ ID NO: 459-461 represent novel genes. The others (SEQ ID NO: 454-458 and 461-467) correspond to known sequences.

EXAMPLE 16

FURTHER CHARACTERIZATION OF PROSTATE-SPECIFIC ANTIGEN P710P

This Example describes the full length cloning of P710P.

The prostate cDNA library described above was screened with the P710P fragment described above. One million colonies were plated on LB/Ampicillin plates. Nylon membrane

filters were used to lift these colonies, and the cDNAs picked up by these filters were then denatured and cross-linked to the filters by UV light. The P710P fragment was radiolabeled and used to hybridize with the filters. Positive cDNA clones were selected and their cDNAs recovered and sequenced by an automatic Perkin Elmer/Applied Biosystems Division Sequencer. Four

5   sequences were obtained, and are presented in SEQ ID NO: 468-471 These sequences appear to represent different splice variants of the P710P gene.

EXAMPLE 17

PROTEIN EXPRESSION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

10

This example describes the expression and purification of the prostate-specific antigen P501S in *E. coli*, baculovirus and mammalian cells.

a)   Expression in *E. coli*

15   Expression of the full-length form of P501S was attempted by first cloning P501S without the leader sequence (amino acids 36-553 of SEQ ID NO: 113) downstream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 (SEQ ID NO: 484) in pET17b. Specifically, P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW003 (SEQ ID NO: 486). AW025 is a sense cloning primer that contains a HindIII site. AW003 is an

20   antisense cloning primer that contains an EcoRI site. DNA amplification was performed using 5 µl 10X Pfu buffer, 1 µl 20 mM dNTPs, 1 µl each of the PCR primers at 10 µM concentration, 40 µl water, 1 µl Pfu DNA polymerase (Stratagene, La Jolla, CA) and 1 µl DNA at 100 ng/µl. Denaturation at 95°C was performed for 30 sec, followed by 10 cycles of 95°C for 30 sec, 60°C for 1 min and by 72°C for 3 min. 20 cycles of 95°C for 30 sec, 65°C for 1 min and by 72°C for 3 min,

25   and lastly by 1 cycle of 72°C for 10 min. The PCR product was cloned to Ra12m/pET17b using HindIII and EcoRI. The sequence of the resulting fusion construct (referred to as Ra12-P501S-F) was confirmed by DNA sequencing.

The fusion construct was transformed into BL21(DE3)pLysE, pLysS and CodonPlus *E. coli* (Stratagene) and grown overnight in LB broth with kanamycin. The resulting culture was

30   induced with IPTG. Protein was transferred to PVDF membrane and blocked with 5% non-fat milk (in PBS-Tween buffer), washed three times and incubated with mouse anti-His tag antibody (Clontech) for 1 hour. The membrane was washed 3 times and probed with HRP-Protein A

(Zymed) for 30 min. Finally, the membrane was washed 3 times and developed with ECL (Amersham). No expression was detected by Western blot. Similarly, no expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage (Invitrogen).

5   An N-terminal fragment of P501S (amino acids 36-325 of SEQ ID NO: 113) was cloned down-stream of the first 30 amino acids of the *M. tuberculosis* antigen Ra12 in pET17b as follows. P501S DNA was used to perform PCR using the primers AW025 (SEQ ID NO: 485) and AW027 (SEQ ID NO: 487). AW027 is an antisense cloning primer that contains an EcoRI site and a stop codon. DNA amplification was performed essentially as described above. The resulting PCR

10   product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The fusion construct (referred to as Ra12-P501S-N) was confirmed by DNA sequencing.

        The Ra12-P501S-N fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, essentially as described above. Using Western blot analysis, protein bands were observed at the expected molecular weight of 36 kDa. Some high molecular weight bands

15   were also observed, probably due to aggregation of the recombinant protein. No expression was detected by Western blot when the Ra12-P501S-F fusion was used for expression in BL21CodonPlus by CE6 phage.

        A fusion construct comprising a C-terminal portion of P501S (amino acids 257-553 of SEQ ID NO: 113) located down-stream of the first 30 amino acids of the *M. tuberculosis* antigen

20   Ra12 (SEQ ID NO: 484) was prepared as follows. P501S DNA was used to perform PCR using the primers AW026 (SEQ ID NO: 488) and AW003 (SEQ ID NO: 486). AW026 is a sense cloning primer that contains a HindIII site. DNA amplification was performed essentially as described above. The resulting PCR product was cloned to Ra12 in pET17b at the HindIII and EcoRI sites. The sequence for the fusion construct (referred to as Ra12-P501S-C) was confirmed.

25   The Ra12-P501S-C fusion construct was used for expression in BL21(DE3)pLysE, pLysS and CodonPlus, as described above. A small amount of protein was detected by Western blot, with some molecular weight aggregates also being observed. Expression was also detected by Western blot when the Ra12-P501S-C fusion was used for expression in BL21CodonPlus induced by CE6 phage.

b)   Expression of P501S in Baculovirus

The Bac-to-Bac baculovirus expression system (BRL Life Technologies, Inc.) was used to express P501S protein in insect cells. Full-length P501S (SEQ ID NO: 113) was amplified by PCR and cloned into the XbaI site of the donor plasmid pFastBacI. The recombinant bacmid and baculovirus were prepared according to the manufacturer's isntructions. The recombinant baculovirus was amplified in Sf9 cells and the high titer viral stocks were utilized to infect High Five cells (Invitrogen) to make the recombinant protein. The identity of the full-length protein was confirmed by N-terminal sequencing of the recombinant protein and by Western blot analysis (Figure 7). Specifically, 0.6 million High Five cells in 6-well plates were infected with either the unrelated control virus BV/ECD_PD (lane 2), with recombinant baculovirus for P501S at different amounts or MOIs (lanes 4-8), or were uninfected (lane 3). Cell lysates were run on SDS-PAGE under reducing conditions and analyzed by Western blot with the anti-P501S monoclonal antibody P501S-10E3-G4D3 (prepared as described below). Lane 1 is the biotinylated protein molecular weight marker (BioLabs).

The localization of recombinant P501S in the insect cells was investigated as follows. The insect cells overexpressing P501S were fractionated into fractions of nucleus, mitochondria, membrane and cytosol. Equal amounts of protein from each fraction were analyzed by Western blot with a monoclonal antibody against P501S. Due to the scheme of fractionation, both nucleus and mitochondria fractions contain some plasma membrane components. However, the membrane fraction is basically free from mitochondria and nucleus. P501S was found to be present in all fractions that contain the membrane component, suggesting that P501S may be associated with plasma membrane of the insect cells expressing the recombinant protein.

c)   Expression of P501S in mammalian cells

Full-length P501S (553AA) was cloned into various mammalian expression vectors, including pCEP4 (Invitrogen), pVR1012 (Vical, San Diego, CA) and a modified form of the retroviral vector pBMN, referred to as pBIB. Transfection of P501S/pCEP4 and P501S/pVR1012 into HEK293 fibroblasts was carried out using the Fugene transfection reagent (Boehringer Mannheim). Briefly, 2 ul of Fugene reagent was diluted into 100 ul of serum-free media and incubated at room temperature for 5-10 min. This mixture was added to 1 ug of P501S plasmid DNA, mixed briefly and incubated for 30 minutes at room temperature. The Fugene/DNA mixture

was added to cells and incubated for 24-48 hours. Expression of recombinant P501S in transfected HEK293 fibroblasts was detected by means of Western blot employing a monoclonal antibody to P501S.

Transfection of p501S/pCEP4 into CHO-K cells (American Type Culture Collection, Rockville, MD) was carried out using GenePorter transfection reagent (Gene Therapy Systems, San Diego, CA). Briefly, 15 μl of GenePorter was diluted in 500 μl of serum-free media and incubated at room temperature for 10 min. The GenePorter/media mixture was added to 2 μg of plasmid DNA that was diluted in 500 μl of serum-free media, mixed briefly and incubated for 30 min at room temperature. CHO-K cells were rinsed in PBS to remove serum proteins, and the GenePorter/DNA mix was added and incubated for 5 hours. The transfected cells were then fed an equal volume of 2x media and incubated for 24-48 hours.

FACS analysis of P501S transiently infected CHO-K cells, demonstrated surface expression of P501S. Expression was detected using rabbit polyclonal antisera raised against a P501S peptide, as described below. Flow cytometric analysis was performed using a FaCScan (Becton Dickinson), and the data were analyzed using the Cell Quest program.

EXAMPLE 18

PREPARATION AND CHARACTERIZATION OF ANTIBODIES AGAINST PROSTATE-SPECIFIC POLYPEPTIDES

a)   Preparation and Characterization of Antibodies against P501S

A murine monoclonal antibody directed against the carboxy-terminus of the prostate-specific antigen P501S was prepared as follows.

A truncated fragment of P501S (amino acids 355-526 of SEQ ID NO: 113) was generated and cloned into the pET28b vector (Novagen) and expressed in *E. coli* as a thioredoxin fusion protein with a histidine tag. The trx-P501S fusion protein was purified by nickel chromatography, digested with thrombin to remove the trx fragment and further purified by an acid precipitation procedure followed by reverse phase HPLC.

Mice were immunized with truncated P501S protein. Serum bleeds from mice that potentially contained anti-P501S polyclonal sera were tested for P501S-specific reactivity using ELISA assays with purified P501S and trx-P501S proteins. Serum bleeds that appeared to react specifically with P501S were then screened for P501S reactivity by Western analysis. Mice that contained a P501S-specific antibody component were sacrificed and spleen cells were used to

generate anti-P501S antibody producing hybridomas using standard techniques. Hybridoma supernatants were tested for P501S-specific reactivity initially by ELISA, and subsequently by FACS analysis of reactivity with P501S transduced cells. Based on these results, a monoclonal hybridoma referred to as 10E3 was chosen for further subcloning. A number of subclones were

5 generated, tested for specific reactivity to P501S using ELISA and typed for IgG isotype. The results of this analysis are shown below in Table V. Of the 16 subclones tested, the monoclonal antibody 10E3-G4-D3 was selected for further study.

<u>Table V</u>

10   <u>Isotype analysis of murine anti-P501S monoclonal antibodies</u>

Hybridoma clone	Isotype	Estimated [Ig] in supernatant (µg/ml)
4D11	IgG1	14.6
1G1	IgG1	0.6
4F6	IgG1	72
4H5	IgG1	13.8
4H5-E12	IgG1	10.7
4H5-EH2	IgG1	9.2
4H5-H2-A10	IgG1	10
4H5-H2-A3	IgG1	12.8
4H5-H2-A10-G6	IgG1	13.6
4H5-H2-B11	IgG1	12.3
10E3	IgG2a	3.4
10E3-D4	IgG2a	3.8
10E3-D4-G3	IgG2a	9.5
10E3-D4-G6	IgG2a	10.4
10E3-E7	IgG2a	6.5
8H12	IgG2a	0.6

The specificity of 10E3-G4-D3 for P501S was examined by FACS analysis.

15 Specifically, cells were fixed (2% formaldehyde, 10 minutes), permeabilized (0.1% saponin, 10 minutes) and stained with 10E3-G4-D3 at 0.5 – 1 µg/ml, followed by incubation with a secondary, FITC-conjugated goat anti-mouse Ig antibody (Pharmingen, San Diego, CA). Cells were then analyzed for FITC fluorescence using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. For analysis of

20 infected cells, B-LCL were infected with a vaccinia vector that expresses P501S. To demonstrate

specificity in these assays, B-LCL transduced with a different antigen (P703P) and uninfected B-LCL vectors were utilized. 10E3-G4-D3 was shown to bind with P501S-transduced B-LCL and also with P501S-infected B-LCL, but not with either uninfected cells or P703P-transduced cells.

To determine whether the epitope recognized by 10E3-G4-D3 was found on the surface or in an intracellular compartment of cells, B-LCL were transduced with P501S or HLA-B8 as a control antigen and either fixed and permeabilized as described above or directly stained with 10E3-G4-D3 and analyzed as above. Specific recognition of P501S by 10E3-G4-D3 was found to require permeabilization, suggesting that the epitope recognized by this antibody is intracellular.

The reactivity of 10E3-G4-D3 with the three prostate tumor cell lines Lncap, PC-3 and DU-145, which are known to express high, medium and very low levels of P501S, respectively, was examined by permeabilizing the cells and treating them as described above. Higher reactivity of 10E3-G4-D3 was seen with Lncap than with PC-3, which in turn showed higher reactivity that DU-145. These results are in agreement with the real time PCR and demonstrate that the antibody specifically recognizes P501S in these tumor cell lines and that the epitope recognized in prostate tumor cell lines is also intracellular.

Specificity of 10E3-G4-D3 for P501S was also demonstrated by Western blot analysis. Lysates from the prostate tumor cell lines Lncap, DU-145 and PC-3, from P501S-transiently transfected HEK293 cells, and from non-transfected HEK293 cells were generated. Western blot analysis of these lysates with 10E3-G4-D3 revealed a 46 kDa immunoreactive band in Lncap, PC-3 and P501S-transfected HEK cells, but not in DU-145 cells or non-transfected HEK293 cells. P501S mRNA expression is consistent with these results since semi-quantitative PCR analysis revealed that P501S mRNA is expressed in Lncap, to a lesser but detectable level in PC-3 and not at all in DU-145 cells. Bacterially expressed and purified recombinant P501S (referred to as P501SStr2) was recognized by 10E3-G4-D3 (24 kDa), as was full-length P501S that was transiently expressed in HEK293 cells using either the expression vector VR1012 or pCEP4. Although the predicted molecular weight of P501S is 60.5 kDa, both transfected and "native" P501S run at a slightly lower mobility due to its hydrophobic nature.

Immunohistochemical analysis was performed on prostate tumor and a panel of normal tissue sections (prostate, adrenal, breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). Tissue samples were fixed in formalin solution for 24 hours and embedded in paraffin before being sliced into 10 micron sections. Tissue sections were permeabilized and incubated with 10E3-G4-D3 antibody for 1 hr.

HRP-labeled anti-mouse followed by incubation with DAB chromogen was used to visualize P501S immunoreactivity. P501S was found to be highly expressed in both normal prostate and prostate tumor tissue but was not detected in any of the other tissues tested.

To identify the epitope recognized by 10E3-G4-D3, an epitope mapping approach
5 was pursued. A series of 13 overlapping 20-21 mers (5 amino acid overlap; SEQ ID NO: 489-501) was synthesized that spanned the fragment of P501S used to generate 10E3-G4-D3. Flat bottom 96 well microtiter plates were coated with either the peptides or the P501S fragment used to immunize mice, at 1 microgram/ml for 2 hours at 37 °C. Wells were then aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature, and
10 subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified antibody 10E3-G4-D3 was added at 2 fold dilutions (1000 ng – 16 ng) in PBST and incubated for 30 minutes at room temperature. This was followed by washing 6 times with PBST and subsequently incubating with HRP-conjugated donkey anti-mouse IgG (H+L)Affinipure F(ab') fragment (Jackson Immunoresearch, West Grove, PA) at 1:20000 for 30 minutes. Plates were then washed and ·
15 incubated for 15 minutes in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 8, reactivity was seen with the peptide of SEQ ID NO: 496 (corresponding to amino acids 439-459 of P501S) and with the P501S fragment but not with the remaining peptides, demonstrating that the epitope recognized by 10E3-G4-D3 is localized to amino acids 439-459 of SEQ ID NO: 113.

20 In order to further evaluate the tissue specificity of P501S, multi-array immunohistochemical analysis was performed on approximately 4700 different human tissues encompassing all the major normal organs as well as neoplasias derived from these tissues. Sixty-five of these human tissue samples were of prostate origin. Tissue sections 0.6 mm in diameter were formalin-fixed and paraffin embedded. Samples were pretreated with HIER using 10 mM
25 citrate buffer pH 6.0 and boiling for 10 min. Sections were stained with 10E3-G4-D3 and P501S immunoreactivity was visualized with HRP. All the 65 prostate tissues samples (5 normal, 55 untreated prostate tumors, 5 hormone refractory prostate tumors) were positive, showing distinct perinuclear staining. All other tissues examined were negative for P501S expression.

30 **b)   Preparation and Characterization of Antibodies against P503S**

A fragment of P503S (amino acids 113-241 of SEQ ID NO: 114) was expressed and purified from bacteria essentially as described above for P501S and used to immunize both rabbits

and mice. Mouse monoclonal antibodies were isolated using standard hybridoma technology as described above. Rabbit monoclonal antibodies were isolated using Selected Lymphocyte Antibody Method (SLAM) technology at Immgenics Pharmaceuticals (Vancouver, BC, Canada). Table VI, below, lists the monoclonal antibodies that were developed against P503S.

5

Table VI

Antibody	Species
20D4	Rabbit
JA1	Rabbit
1A4	Mouse
1C3	Mouse
1C9	Mouse
1D12	Mouse
2A11	Mouse
2H9	Mouse
4H7	Mouse
8A8	Mouse
8D10	Mouse
9C12	Mouse
6D12	Mouse

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 20D4 and JA1 were determined and are provided in SEQ ID NO: 502 and 503, respectively.

In order to better define the epitope binding region of each of the antibodies, a series of overlapping peptides were generated that span amino acids 109-213 of SEQ ID NO: 114. These peptides were used to epitope map the anti-P503S monoclonal antibodies by ELISA as follows. The recombinant fragment of P503S that was employed as the immunogen was used as a positive control. Ninety-six well microtiter plates were coated with either peptide or recombinant antigen at 20 ng/well overnight at 4 °C. Plates were aspirated and blocked with phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature then washed in PBS containing 0.1% Tween 20 (PBST). Purified rabbit monoclonal antibodies diluted in PBST were added to the wells and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubation with Protein-A HRP conjugate at a 1:2000 dilution for a further 30 min. Plates were washed six times in PBST and incubated with tetramethylbenzidine (TMB) substrate for a further

15 min. The reaction was stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using at ELISA plate reader. ELISA with the mouse monoclonal antibodies was performed with supernatants from tissue culture run neat in the assay.

All of the antibodies bound to the recombinant P503S fragment, with the exception

5   of the negative control SP2 supernatant. 20D4, JA1 and 1D12 bound strictly to peptide #2101 (SEQ ID NO: 504), which corresponds to amino acids 151-169 of SEQ ID NO: 114. 1C3 bound to peptide #2102 (SEQ ID NO: 505), which corresponds to amino acids 165-184 of SEQ ID NO: 114. 9C12 bound to peptide #2099 (SEQ ID NO: 522), which corresponds to amino acids 120-139 of SEQ ID NO: 114. The other antibodies bind to regions that were not examined in these studies.

10 Subsequent to epitope mapping, the antibodies were tested by FACS analysis on a cell line that stably expressed P503S to confirm that the antibodies bind to cell surface epitopes. Cells stably transfected with a control plasmid were employed as a negative control. Cells were stained live with no fixative. 0.5 ug of anti-P503S monoclonal antibody was added and cells were incubated on ice for 30 min before being washed twice and incubated with a FITC-labelled goat

15 anti-rabbit or mouse secondary antibody for 20 min. After being washed twice, cells were analyzed with an Excalibur fluorescent activated cell sorter. The monoclonal antibodies 1C3, 1D12, 9C12, 20D4 and JA1, but not 8D3, were found to bind to a cell surface epitope of P503S.

In order to determine which tissues express P503S, immunohistochemical analysis was performed, essentially as described above, on a panel of normal tissues (prostate, adrenal,

20 breast, cervix, colon, duodenum, gall bladder, ileum, kidney, ovary, pancreas, parotid gland, skeletal muscle, spleen and testis). HRP-labeled anti-mouse or anti-rabbit antibody followed by incubation with TMB was used to visualize P503S immunoreactivity. P503S was found to be highly expressed in prostate tissue, with lower levels of expression being observed in cervix, colon, ileum and kidney, and no expression being observed in adrenal, breast, duodenum, gall bladder, ovary,

25 pancreas, parotid gland, skeletal muscle, spleen and testis.

Western blot analysis was used to characterize anti-P503S monoclonal antibody specificity. SDS-PAGE was performed on recombinant (rec) P503S expressed in and purified from bacteria and on lysates from HEK293 cells transfected with full length P503S. Protein was transferred to nitrocellulose and then Western blotted with each of the anti-P503S monoclonal

30 antibodies (20D4, JA1, 1D12, 6D12 and 9C12) at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to either a goat anti-mouse monoclonal antibody or to protein A-sepharose. The monoclonal antibody 20D4 detected the

appropriate molecular weight 14 kDa recombinant P503S (amino acids 113-241) and the 23.5 kDa species in the HEK293 cell lysates transfected with full length P503S.   Other anti-P503S monoclonal antibodies displayed similar specificity by Western blot.

5   **c) Preparation and Characterization of Antibodies against P703P**

Rabbits were immunized with either a truncated (P703Ptr1; SEQ ID NO: 172) or full-length mature form (P703Pfl; SEQ ID NO: 523) of recombinant P703P protein was expressed in and purified from bacteria as described above. Affinity purified polyclonal antibody was generated using immunogen P703Pfl or P703Ptr1 attached to a solid support. Rabbit monoclonal
10   antibodies were isolated using SLAM technology at Immgenics Pharmaceuticals. Table VII below lists both the polyclonal and monoclonal antibodies that were generated against P703P.

Table VII

Antibody	Immunogen	Species/type
Aff. Purif. P703P (truncated); #2594	P703Ptrl	Rabbit polyclonal
Aff. Purif. P703P (full length); #9245	P703Pfl	Rabbit polyclonal
2D4	P703Ptrl	Rabbit monoclonal
8H2	P703Ptrl	Rabbit monoclonal
7H8	P703Ptrl	Rabbit monoclonal

15

The DNA sequences encoding the complementarity determining regions (CDRs) for the rabbit monoclonal antibodies 8H2, 7H8 and 2D4 were determined and are provided in SEQ ID NO: 506-508, respectively.

Epitope mapping studies were performed as described above.   Monoclonal
20   antibodies 2D4 and 7H8 were found to specifically bind to the peptides of SEQ ID NO: 509 (corresponding to amino acids 145-159 of SEQ ID NO: 172) and SEQ ID NO: 510 (corresponding to amino acids 11-25 of SEQ ID NO: 172), respectively. The polyclonal antibody 2594 was found to bind to the peptides of SEQ ID NO: 511-514, with the polyclonal antibody 9427 binding to the peptides of SEQ ID NO: 515-517.

25   The specificity of the anti-P703P antibodies was determined by Western blot analysis as follows. SDS-PAGE was performed on (1) bacterially expressed recombinant antigen; (2) lysates of HEK293 cells and Ltk-/- cells either untransfected or transfected with a plasmid

expressing full length P703P; and (3) supernatant isolated from these cell cultures. Protein was transferred to nitrocellulose and then Western blotted using the anti-P703P polyclonal antibody #2594 at an antibody concentration of 1 ug/ml. Protein was detected using horse radish peroxidase (HRP) conjugated to an anti-rabbit antibody. A 35 kDa immunoreactive band could be observed

5   with recombinant P703P. Recombinant P703P runs at a slightly higher molecular weight since it is epitope tagged. In lysates and supernatants from cells transfected with full length P703P, a 30 kDa band corresponding to P703P was observed. To assure specificity, lysates from HEK293 cells stably transfected with a control plasmid were also tested and were negative for P703P expression. Other anti-P703P antibodies showed similar results.

10   Immunohistochemical studies were performed as described above, using anti-P703P monoclonal antibody. P703P was found to be expressed at high levels in normal prostate and prostate tumor tissue but was not detectable in all other tissues tested (breast tumor, lung tumor and normal kidney).

15   EXAMPLE 19

CHARACTERIZATION OF CELL SURFACE EXPRESSION AND CHROMOSOME
LOCALIZATION OF THE PROSTATE-SPECIFIC ANTIGEN P501S

            This example describes studies demonstrating that the prostate-specific antigen

20   P501S is expressed on the surface of cells, together with studies to determine the probable chromosomal location of P501S.

            The protein P501S (SEQ ID NO: 113) is predicted to have 11 transmembrane domains. Based on the discovery that the epitope recognized by the anti-P501S monoclonal antibody 10E3-G4-D3 (described above in Example 17) is intracellular, it was predicted that

25   following transmembrane determinants would allow the prediction of extracellular domains of P501S. Fig. 9 is a schematic representation of the P501S protein showing the predicted location of the transmembrane domains and the intracellular epitope described in Example 17. Underlined sequence represents the predicted transmembrane domains, bold sequence represents the predicted extracellular domains, and italized sequence represents the predicted intracellular domains.

30   Sequence that is both bold and underlined represents sequence employed to generate polyclonal rabbit serum. The location of the transmembrane domains was predicted using HHMTOP as

described by Tusnady and Simon (Principles Governing Amino Acid Composition of Integral Membrane Proteins: Applications to Topology Prediction, *J. Mol. Biol. 283*:489-506, 1998).

Based on Fig. 9, the P501S domain flanked by the transmembrane domains corresponding to amino acids 274-295 and 323-342 is predicted to be extracellular. The peptide of
5 SEQ ID NO: 518 corresponds to amino acids 306-320 of P501S and lies in the predicted extracellular domain. The peptide of SEQ ID NO: 519, which is identical to the peptide of SEQ ID NO: 518 with the exception of the substitution of the histidine with an asparginine, was synthesized as described above. A Cys-Gly was added to the C-terminus of the peptide to facilitate conjugation to the carrier protein. Cleavage of the peptide from the solid support was carried out using the
10 following cleavage mixture: trifluoroacetic acid:ethanediol:thioanisol:water:phenol (40:1:2:2:3). After cleaving for two hours, the peptide was precipitated in cold ether. The peptide pellet was then dissolved in 10% v/v acetic acid and lyophilized prior to purification by C18 reverse phase hplc. A gradient of 5-60% acetonitrile (containing 0.05% TFA) in water (containing 0.05% TFA) was used to elute the peptide. The purity of the peptide was verified by hplc and mass spectrometry, and was
15 determined to be >95%. The purified peptide was used to generate rabbit polyclonal antisera as described above.

Surface expression of P501S was examined by FACS analysis. Cells were stained with the polyclonal anti-P501S peptide serum at 10 μg/ml, washed, incubated with a secondary FITC-conjugated goat anti-rabbit Ig antibody (ICN), washed and analyzed for FITC fluorescence
20 using an Excalibur fluorescence activated cell sorter. For FACS analysis of transduced cells, B-LCL were retrovirally transduced with P501S. To demonstrate specificity in these assays, B-LCL transduced with an irrelevant antigen (P703P) or nontransduced were stained in parallel. For FACS analysis of prostate tumor cell lines, Lncap, PC-3 and DU-145 were utilized. Prostate tumor cell lines were dissociated from tissue culture plates using cell dissociation medium and stained as
25 above. All samples were treated with propidium iodide (PI) prior to FACS analysis, and data was obtained from PI-excluding (i.e. intact and non-permeabilized) cells. The rabbit polyclonal serum generated against the peptide of SEQ ID NO: 519 was shown to specifically recognize the surface of cells transduced to express P501S, demonstrating that the epitope recognized by the polyclonal serum is extracellular.

30 To determine biochemically if P501S is expressed on the cell surface, peripheral membranes from Lncap cells were isolated and subjected to Western blot analysis. Specifically, Lncap cells were lysed using a dounce homogenizer in 5 ml of homogenization buffer (250 mM

sucrose, 10 mM HEPES, 1mM EDTA, pH 8.0, 1 complete protease inhibitor tablet (Boehringer Mannheim)). Lysate samples were spun at 1000 g for 5 min at 4 °C. The supernatant was then spun at 8000g for 10 min at 4 °C. Supernatant from the 8000g spin was recovered and subjected to a 100,000g spin for 30 min at 4 °C to recover peripheral membrane. Samples were then separated by

5 SDS-PAGE and Western blotted with the mouse monoclonal antibody 10E3-G4-D3 (described above in Example 17) using conditions described above. Recombinant purified P501S, as well as HEK293 cells transfected with and over-expressing P501S were included as positive controls for P501S detection. LCL cell lysate was included as a negative control. P501S could be detected in Lncap total cell lysate, the 8000g (internal membrane) fraction and also in the 100,000g (plasma

10 membrane) fraction. These results indicate that P501S is expressed at, and localizes to, the peripheral membrane.

To demonstrate that the rabbit polyclonal antiserum generated to the peptide of SEQ ID NO: 519 specifically recognizes this peptide as well as the corresponding native peptide of SEQ ID NO: 518, ELISA analyses were performed. For these analyses, flat-bottomed 96 well microtiter

15 plates were coated with either the peptide of SEQ ID NO: 519, the longer peptide of SEQ ID NO: 520 that spans the entire predicted extracellular domain, the peptide of SEQ ID NO: 521 which represents the epitope recognized by the P501S-specific antibody 10E3-G4-D3, or a P501S fragment (corresponding to amino acids 355-526 of SEQ ID NO: 113) that does not include the immunizing peptide sequence, at 1 μg/ml for 2 hours at 37 °C. Wells were aspirated, blocked with

20 phosphate buffered saline containing 1% (w/v) BSA for 2 hours at room temperature and subsequently washed in PBS containing 0.1% Tween 20 (PBST). Purified anti-P501S polyclonal rabbit serum was added at 2 fold dilutions (1000 ng - 125 ng) in PBST and incubated for 30 min at room temperature. This was followed by washing 6 times with PBST and incubating with HRP-conjugated goat anti-rabbit IgG (H+L) Affinipure F(ab') fragment at 1:20000 for 30 min. Plates

25 were then washed and incubated for 15 min in tetramethyl benzidine. Reactions were stopped by the addition of 1N sulfuric acid and plates were read at 450 nm using an ELISA plate reader. As shown in Fig. 11, the anti-P501S polyclonal rabbit serum specifically recognized the peptide of SEQ ID NO: 519 used in the immunization as well as the longer peptide of SEQ ID NO: 520, but did not recognize the irrelevant P501S-derived peptides and fragments.

30 In further studies, rabbits were immunized with peptides derived from the P501S sequence and predicted to be either extracellular or intracellular, as shown in Fig. 9. Polyclonal rabbit sera were isolated and polyclonal antibodies in the serum were purified, as described above.

To determine specific reactivity with P501S, FACS analysis was employed, utilizing either B-LCL transduced with P501S or the irrelevant antigen P703P, of B-LCL infected with vaccinia virus-expressing P501S. For surface expression, dead and non-intact cells were excluded from the analysis as described above. For intracellular staining, cells were fixed and permeabilized as described above. Rabbit polyclonal serum generated against the peptide of SEQ ID NO: 548, which corresponds to amino acids 181-198 of P501S, was found to recognize a surface epitope of P501S. Rabbit polyclonal serum generated against the peptide SEQ ID NO: 551, which corresponds to amino acids 543-553 of P501S, was found to recognize an epitope that was either potentially extracellular or intracellular since in different experiments intact or permeabilized cells were recognized by the polyclonal sera. Based on similar deductive reasoning, the sequences of SEQ ID NO: 541-547, 549 and 550, which correspond to amino acids 109-122, 539-553, 509-520, 37-54, 342-359, 295-323, 217-274, 143-160 and 75-88, respectively, of P501S, can be considered to be potential surface epitopes of P501S recognized by antibodies.

The chromosomal location of P501S was determined using the GeneBridge 4 Radiation Hybrid panel (Research Genetics). The PCR primers of SEQ ID NO: 528 and 529 were employed in PCR with DNA pools from the hybrid panel according to the manufacturer's directions. After 38 cycles of amplification, the reaction products were separated on a 1.2% agarose gel, and the results were analyzed through the Whitehead Institute/MIT Center for Genome Research web server (http://www-genome.wi.mit.edu/cgi-bin/contig/rhmapper.pl) to determine the probable chromosomal location. Using this approach, P501S was mapped to the long arm of chromosome 1 at WI-9641 between q32 and q42. This region of chromosome 1 has been linked to prostate cancer susceptibility in hereditary prostate cancer (Smith et al. Science 274:1371-1374, 1996 and Berthon et al. Am. J. Hum. Genet. 62:1416-1424, 1998). These results suggest that P501S may play a role in prostate cancer malignancy.

From the foregoing, it will be appreciated that, although specific embodiments of the invention have been described herein for the purposes of illustration, various modifications may be made without deviating from the spirit and scope of the invention. Accordingly, the present invention is not limited except as by the appended claims.

CLAIMS

1.   An isolated polypeptide comprising at least an immunogenic portion of a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(a)   sequences recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536;

(b)   sequences that hybridize to any of the foregoing sequences under moderately stringent conditions; and

(c)   complements of any of the sequence of (a) or (b).

2.   An isolated polypeptide according to claim 1, wherein the polypeptide comprises an amino acid sequence that is encoded by a polynucleotide sequence recited in any one of SEQ ID No: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotide sequences.

3.   An isolated polypeptide comprising a sequence recited in any one of SEQ ID NO: 108, 112, 113, 114, 172, 176, 178, 327, 329, 331, 339, 383, 477-483, 496, 504, 505, 519, 520, 522, 525, 527, 532, 534 and 537-550.

4.   An isolated polynucleotide encoding at least 15 contiguous amino acid residues of a prostate-specific protein, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with antigen-specific antisera is not substantially diminished, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

5.   An isolated polynucleotide encoding a prostate-specific protein, or a variant thereof, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing sequences.

6.   An isolated polynucleotide comprising a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

7.   An isolated polynucleotide comprising a sequence that hybridizes under moderately stringent conditions to a sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536.

8.   An isolated polynucleotide complementary to a polynucleotide according to any one of claims 4-7.

9.   An expression vector comprising a polynucleotide according to any one of claims 4-8.

10.   A host cell transformed or transfected with an expression vector according to claim 9.

11.   An isolated antibody, or antigen-binding fragment thereof, that specifically binds to a prostate-specific protein, the protein comprising an amino acid sequence encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389, 390, 392, 393, 396, 401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450, 452, 453, 459-461, 468-471, 472-476, 524, 526, 530, 531, 533, 535 and 536 or a complement of any of the foregoing polynucleotide sequences.

12. A monoclonal antibody that specifically binds to an amino acid sequence selected from the group consisting of SEQ ID NO: 496, 504, 505, 509-517, 519, 520, 522 and 539-551.

5   13. A monoclonal antibody comprising a complementarity determining region selected from the group consisting of SEQ ID NO: 502, 503 and 506-508.

14. A fusion protein comprising at least one polypeptide according to 10   claim 1.

15. A fusion protein according to claim 14, wherein the fusion protein comprises an expression enhancer that increases expression of the fusion protein in a host cell transfected with a polynucleotide encoding the fusion protein.

15

16. A fusion protein according to claim 14, wherein the fusion protein comprises a T helper epitope that is not present within the polypeptide of claim 1.

17. A fusion protein according to claim 14, wherein the fusion protein 20   comprises an affinity tag.

18. An isolated polynucleotide encoding a fusion protein according to claim 14.

25   19.. A pharmaceutical composition comprising a physiologically acceptable carrier and at least one component selected from the group consisting of:

    (a) a polypeptide according to claim 1;

    (b) a polynucleotide according to claim 4;

    (c) an antibody according to any one of claims 11-13;

30   (d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

20.   A vaccine comprising an immunostimulant and at least one component selected from the group consisting of:

(a) a polypeptide according to claim 1;

(b) a polynucleotide according to claim 4;

(c) an antibody according to any one of claims 11-13;

(d) a fusion protein according to claim 14; and

(e) a polynucleotide according to claim 18.

21.   A vaccine according to claim 20, wherein the immunostimulant is an adjuvant.

22.   A vaccine according to claim 20, wherein the immunostimulant induces a predominantly Type I response.

23.   A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a pharmaceutical composition according to claim 19.

24.   A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a vaccine according to claim 20.

25.   A pharmaceutical composition comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with a pharmaceutically acceptable carrier or excipient.

26.   A pharmaceutical composition according to claim 25, wherein the antigen presenting cell is a dendritic cell or a macrophage.

27.   A vaccine comprising an antigen-presenting cell that expresses a polypeptide according to claim 1, in combination with an immunostimulant.

5   28.   A vaccine according to claim 27, wherein the immunostimulant is an adjuvant.

29.   A vaccine according to claim 27, wherein the immunostimulant induces a predominantly Type I response.

10

30.   A vaccine according to claim 27, wherein the antigen-presenting cell is a dendritic cell.

31.   A method for inhibiting the development of a cancer in a patient, 15 comprising administering to a patient an effective amount of an antigen-presenting cell that expresses a polypeptide encoded by a polynucleotide recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, and thereby inhibiting the development of a cancer in the patient.

20

32.   A method according to claim 31, wherein the antigen-presenting cell is a dendritic cell.

33.   A method according to any one of claims 23, 24 and 31, wherein the 25 cancer is prostate cancer.

34.   A method for removing tumor cells from a biological sample, comprising contacting a biological sample with T cells that specifically react with a prostate-specific protein, wherein the protein comprises an amino acid sequence that is 30 encoded by a polynucleotide sequence selected from the group consisting of:

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(i)   polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii)   complements of the foregoing polynucleotides;

wherein the step of contacting is performed under conditions and for a time sufficient to permit the removal of cells expressing the prostate-specific protein from the sample.

35.   A method according to claim 34, wherein the biological sample is blood or a fraction thereof.

36.   A method for inhibiting the development of a cancer in a patient, comprising administering to a patient a biological sample treated according to the method of claim 50.

37.   A method for stimulating and/or expanding T cells specific for a prostate-specific protein, comprising contacting T cells with at least one component selected from the group consisting of:

(i)   a polypeptide according to claim 1;

(ii)   a polypeptide encoded by a polynucleotide comprising a sequence provided in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii)   a polynucleotide encoding a polypeptide of (i) or (ii); and

(iv)   an antigen presenting cell that expresses a polypeptide of (i) or (ii),

under conditions and for a time sufficient to permit the stimulation and/or expansion of T cells.

38.   An isolated T cell population, comprising T cells prepared according to the method of claim 37.

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39.   A method for inhibiting the development of a cancer in a patient, comprising administering to a patient an effective amount of a T cell population according to claim 38.

5   40.   A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a)   incubating CD4$^+$ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

(i)   a polypeptide according to claim 1;

10   (ii)   a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

(iii)   a polynucleotide encoding a polypeptide of (i) or (ii); or

15   (iv)   an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate; and

(b)   administering to the patient an effective amount of the proliferated T cells, and thereby inhibiting the development of a cancer in the patient.

20

41.   A method for inhibiting the development of a cancer in a patient, comprising the steps of:

(a)   incubating CD4$^+$ and/or CD8+ T cells isolated from a patient with at least one component selected from the group consisting of:

25   (i)   a polypeptide according to claim 1;

(ii)   a polypeptide encoded by a polynucleotide comprising a sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536;

30   (iii)   a polynucleotide encoding a polypeptide of (i) or (ii); or

(iv)   an antigen-presenting cell that expresses a polypeptide of (i) or (ii);

such that T cells proliferate;

(b)   cloning at least one proliferated cell to provide cloned T cells; and

(c)   administering to the patient an effective amount of the cloned T cells, and thereby inhibiting the development of a cancer in the patient.

42.   A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a)   contacting a biological sample obtained from a patient with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence selected from the group consisting of:

(i)   polynucleotides recited in any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536; and

(ii)   complements of the foregoing polynucleotides;

(b)   detecting in the sample an amount of polypeptide that binds to the binding agent; and

(c)   comparing the amount of polypeptide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

43.   A method according to claim 42, wherein the binding agent is an antibody.

44.   A method according to claim 43, wherein the antibody is a monoclonal antibody.

45.   A method according to claim 42, wherein the cancer is prostate cancer.

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46.   A method for monitoring the progression of a cancer in a patient, comprising the steps of:

(a)   contacting a biological sample obtained from a patient at a first point in time with a binding agent that binds to a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

(b)   detecting in the sample an amount of polypeptide that binds to the binding agent;

(c)   repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent point in time; and

(d)   comparing the amount of polypeptide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

47.   A method according to claim 46, wherein the binding agent is an antibody.

48.   A method according to claim 47, wherein the antibody is a monoclonal antibody.

49.   A method according to claim 46, wherein the cancer is a prostate cancer.

50.   A method for determining the presence or absence of a cancer in a patient, comprising the steps of:

(a)   contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein,

110

wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315, 326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

5   (b)   detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide; and

               (c)   comparing the amount of polynucleotide that hybridizes to the oligonucleotide to a predetermined cut-off value, and therefrom determining the presence or absence of a cancer in the patient.

10

               51.   A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

15   52.   A method according to claim 50, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

               53.   A method for monitoring the progression of a cancer in a patient,
20   comprising the steps of:

               (a)   contacting a biological sample obtained from a patient with an oligonucleotide that hybridizes to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is encoded by a polynucleotide sequence of any one of SEQ ID NO: 1-111, 115-171, 173-175, 177, 179-305, 307-315,
25   326, 328, 330, 332-335, 340-375, 381, 382 and 384-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any of the foregoing polynucleotides;

               (b)   detecting in the sample an amount of a polynucleotide that hybridizes to the oligonucleotide;

               (c)   repeating steps (a) and (b) using a biological sample obtained from
30   the patient at a subsequent point in time; and

111

(d)   comparing the amount of polynucleotide detected in step (c) to the amount detected in step (b) and therefrom monitoring the progression of the cancer in the patient.

5   54.   A method according to claim 53, wherein the amount of polynucleotide that hybridizes to the oligonucleotide is determined using a polymerase chain reaction.

           55.   A method according to claim 53, wherein the amount of
10   polynucleotide that hybridizes to the oligonucleotide is determined using a hybridization assay.

           56.   A diagnostic kit, comprising:

           (a)   one or more antibodies according to claim 11; and

15   (b)   a detection reagent comprising a reporter group.

           57.   A kit according to claim 56, wherein the antibodies are immobilized on a solid support.

20   58.   A kit according to claim 56, wherein the detection reagent comprises an anti-immunoglobulin, protein G, protein A or lectin.

           59.   A kit according to claim 56, wherein the reporter group is selected from the group consisting of radioisotopes, fluorescent groups, luminescent groups,
25   enzymes, biotin and dye particles.

           60.   An oligonucleotide comprising 10 to 40 contiguous nucleotides that hybridize under moderately stringent conditions to a polynucleotide that encodes a prostate-specific protein, wherein the protein comprises an amino acid sequence that is
30   encoded by a polynucleotide sequence recited in any one of SEQ ID NO: 2, 3, 8-29, 41-45,

47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-111, 115-160, 171,

173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220, 222-225, 227-305,

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401, 402, 407, 408, 410, 413, 415-419, 422, 426, 427, 432, 434, 435, 442-444, 446, 450,

5   452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536, or a complement of any

of the foregoing polynucleotides.

61.   A oligonucleotide according to claim 60, wherein the

oligonucleotide comprises 10-40 contiguous nucleotides recited in any one of SEQ ID NO:

10   2, 3, 8-29, 41-45, 47-52, 54-65, 70, 73-74, 79, 81, 87, 90, 92, 93, 97, 103, 104, 107, 109-

111, 115-160, 171, 173-175, 177, 181, 188, 191, 193, 194, 198, 203, 204, 207, 209, 220,

222-225, 227-305, 307-315, 326, 328, 330, 332, 334, 350-365, 381, 382, 384, 386, 389,

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442-444, 446, 450, 452, 453, 459-461, 468-476, 524, 526, 530, 531, 533, 535 and 536.

15

62.   A diagnostic kit, comprising:

(a)   an oligonucleotide according to claim 61; and

(b)   a diagnostic reagent for use in a polymerase chain reaction or

hybridization assay.

20

63.   A host cell according to claim 10, wherein the cell is selected from

the group consisting of: *E. coli*, baculovirus and mammalian cells.

64.   A recombinant protein produced by a host cell according to claim

25   10.
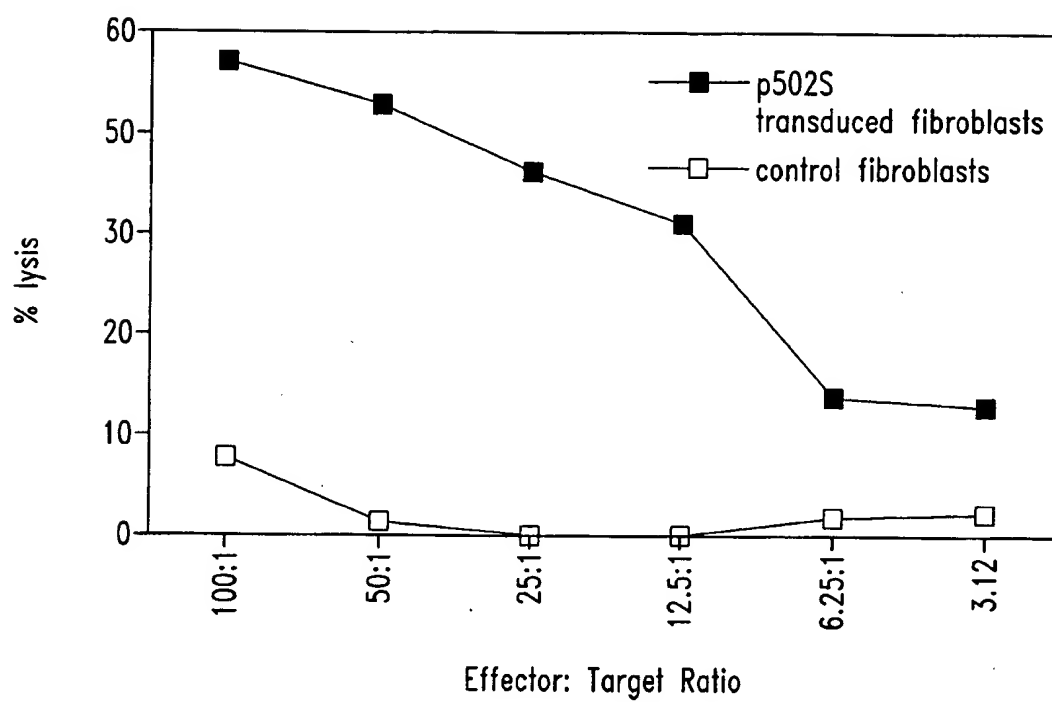
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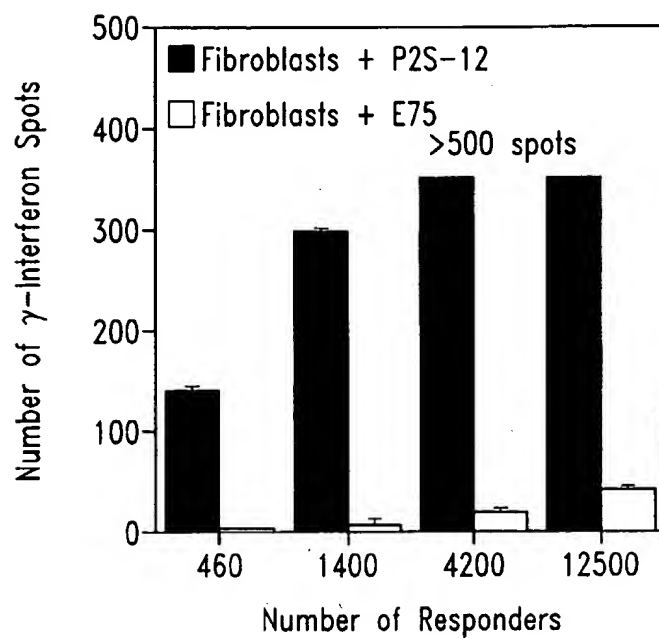
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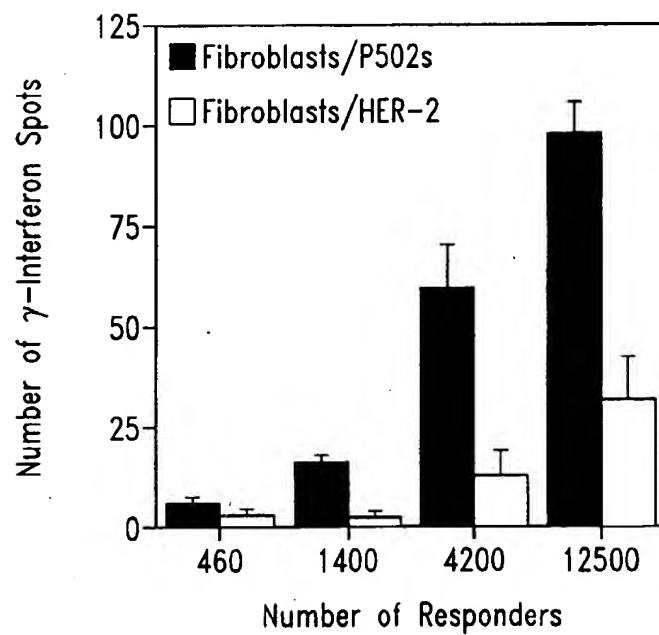
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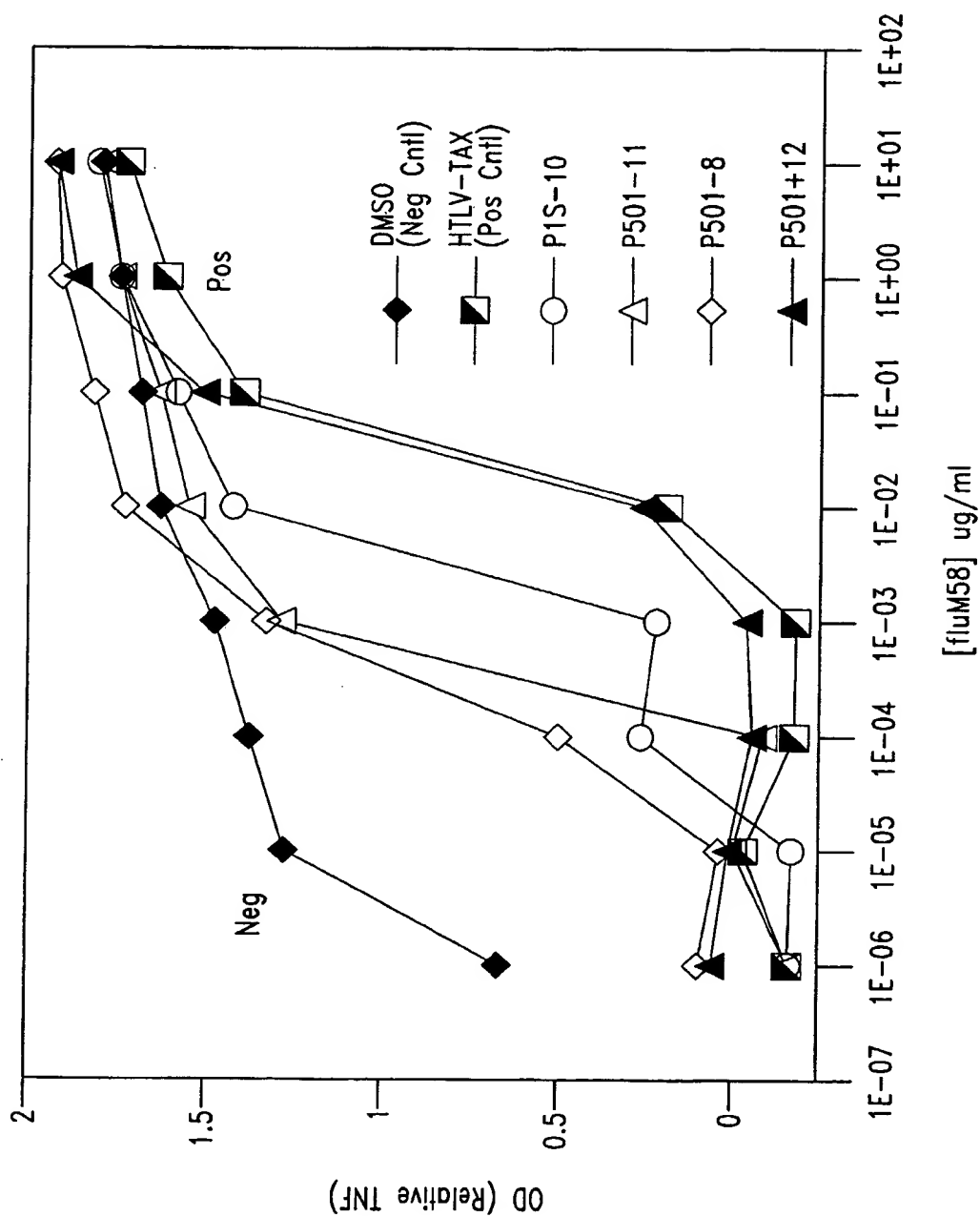
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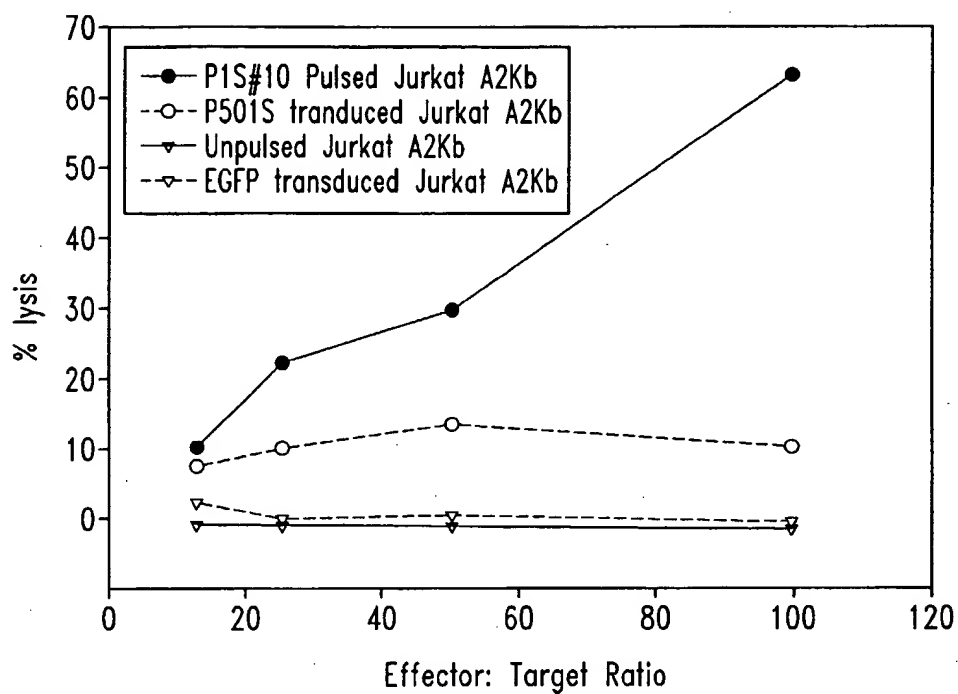
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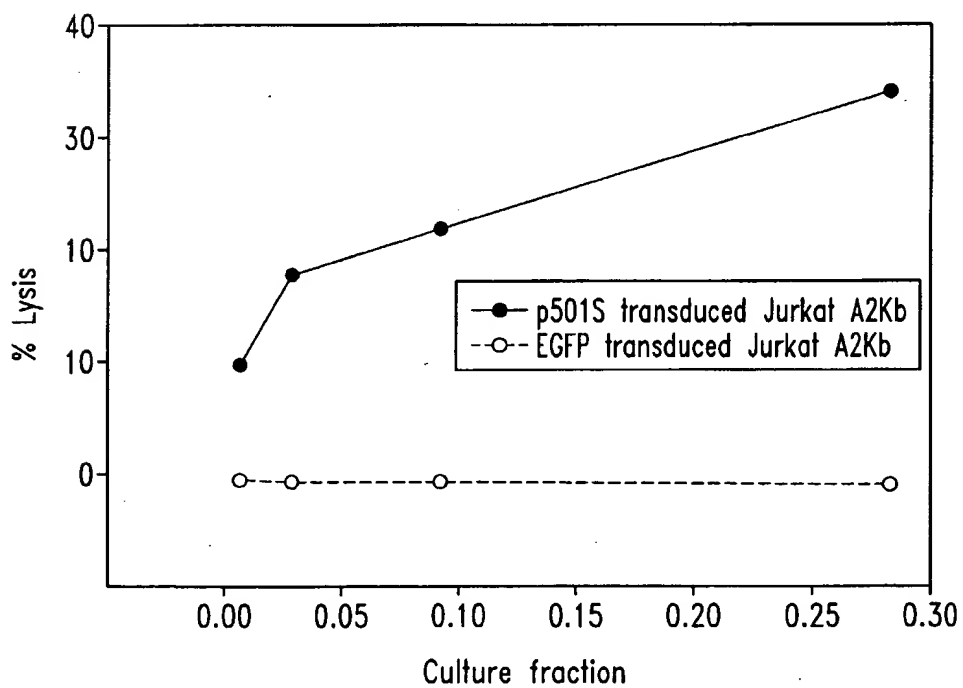
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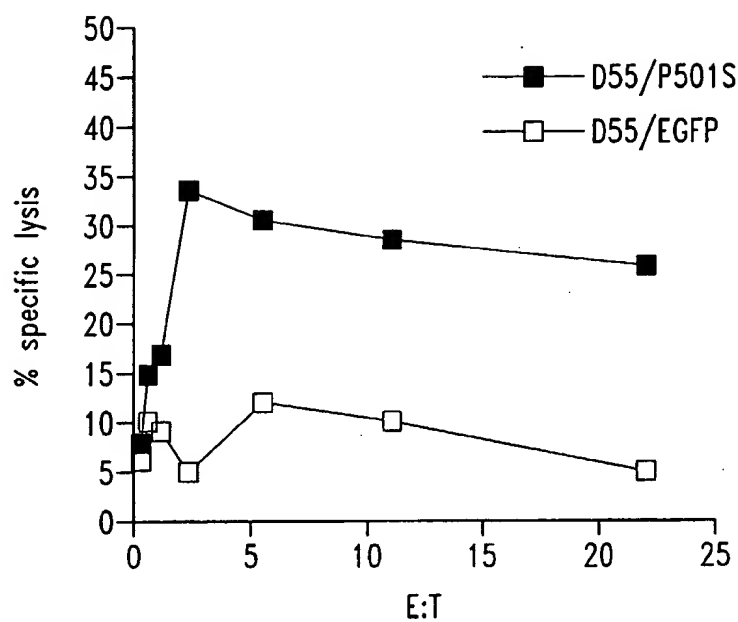
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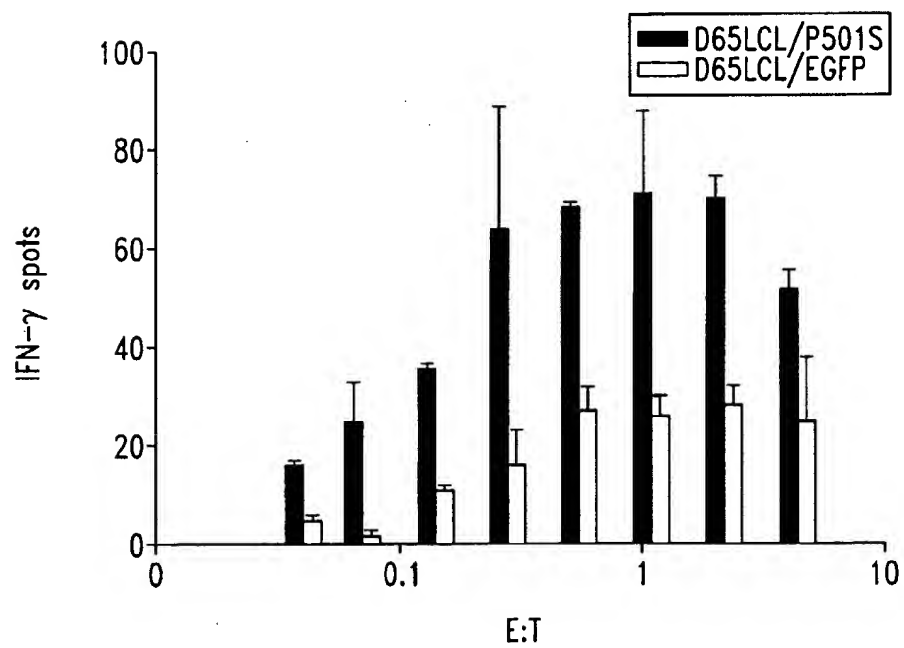
Fig. 6B

Expression of P501S
by the Baculovirus Expression System
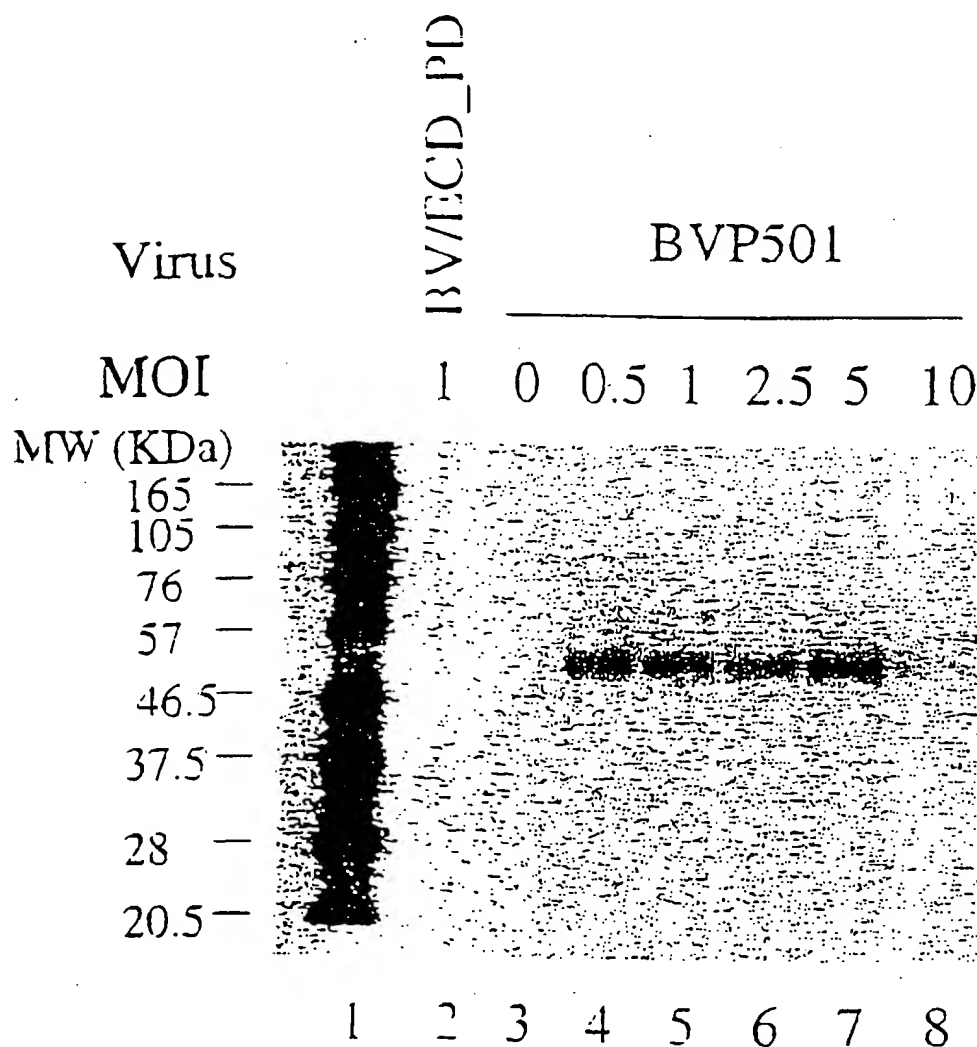
0.6 million high 5 cells in 6-well plate were infected with an unrelated control virus BV/ECD_PD (lane 2), without virus (lane 3), or with recombinant baculovirus for P501 at different MOIs (lane 4 – 8). Cell lysates were run on SDS-PAGE under the reducing conditions and analyzed by Western blot with a monoclonal antibody against P501 S (P501S-10E3-G4D3). Lane 1 is the biotinylated protein molecular weight marker (BioRads).

Fig. 7

Figure 8. Mapping of the epitope recognized by 10E3-G4-D3

Fig. 8

Schematic of P501S with predicted
transmembrane, cytoplasmic, and extracellular regions

MVQRLWVSRLLRHRK AQLLLVNLLTFGLEVCLAAGIT **YVPPLLLEVGVEEKFM**
TMVLGIGPVLGLVCYPLLGSAS

DHWRGRYGRRRP FIWALSLGILLSLFLIPRAGWL **AGLLCPDPRPLE** LALLILGVGLLDFCGQVCFTPL

EALLSDLFRDPDHCRQ AYSVYAFMISLGGCLGYLLPAI **DWDTSALAPYLGTQEE**

CLFGLLTLIFLTCVAATLLV *AEEAALGPTEPAEGLSAPSLSPHCCPCRARLAFRNLGALLPRL*

HQLCCRMPRTLRR LFVAELCSWMALMTFTLFYTDF **VGEGLYQGVPRAEPGTEARRHYDEGVR**

MGSLGLFLQCAISLVFSLVM *DRLVQRFGTRAVYLAS* VAAFPVAAGATCLSHSVAVVTA **SAA**

LTGFTFSALQILPYTLASLY *HREKQVFLPKYRGDTGGASSEDSLMTSFLPGPKPGAPFPNGHVGAGGSGL*

LPPPPALCGASACDVSVRVVVGEPTEARVVPGRG ICLDLAILDSAFLLSQVAPSLF **MGSIVQLSQS**

VTAYMVSAAGLGLVAIYFAT *QVVFDKSDLAKYSA*

Underlined sequence: Predicted transmembrane domain; **Bold sequence**:
Predicted extracellular domain; *Italic sequence*: Predicted intracellular
domain. Sequence in bold/underlined: used generate polyclonal rabbit
serum

Localization of domains predicted using HMMTOP (G.E. Tusnady an I. Simon
(1998) Principles Governing Amino Acid Composition of Integral Membrane
Proteins: Applications to topology Prediction.J.Mol Biol. 283, 489-506.

Fig. 9

Fig. 10

Elisa assay of rabbit polyclonal
antibody specificity

■— P501S 306-320 RAEPGTEARRNYDEG(cg)
◆— P501S 296-320: (gc)VGEGLYQGVPRAEPGTEARRHYDEG
△— P501S 439-459
○— P501S FRAGMENT 343-525

Fig. 11

ng mouse polyclonal serum

O.D.450
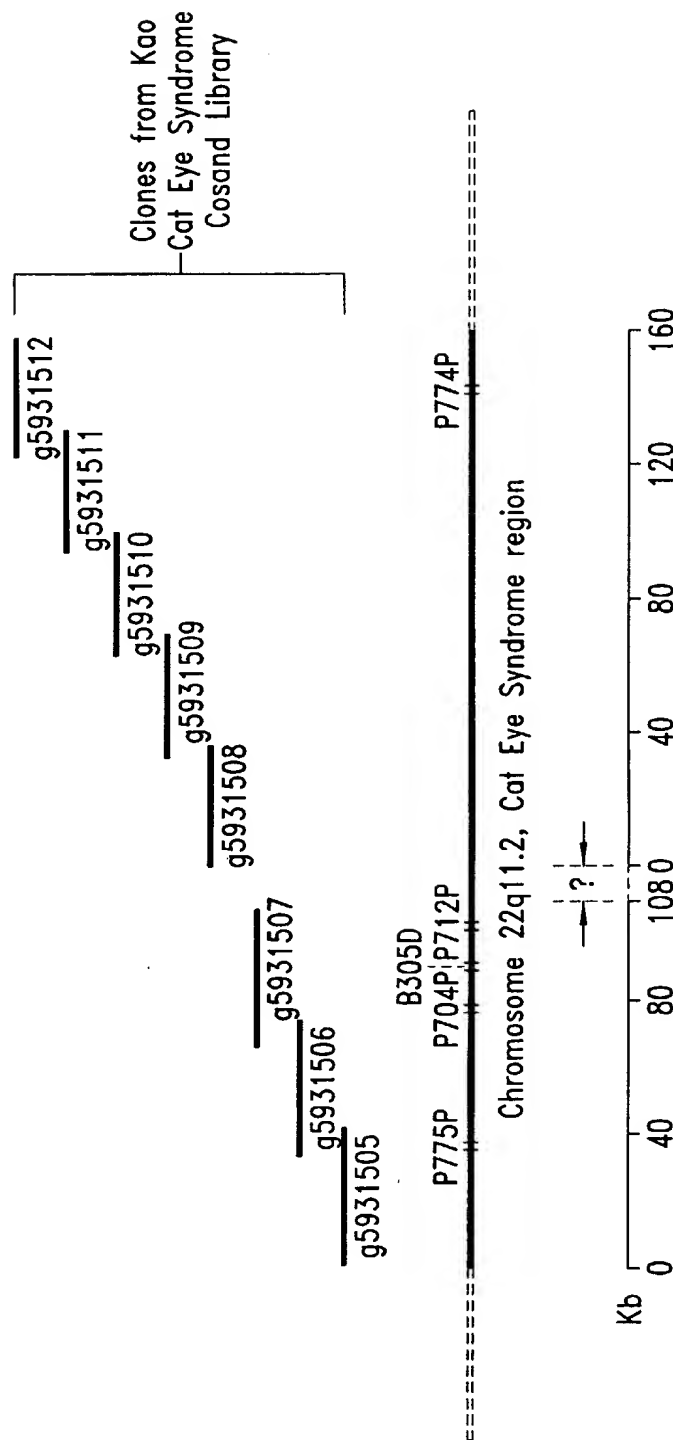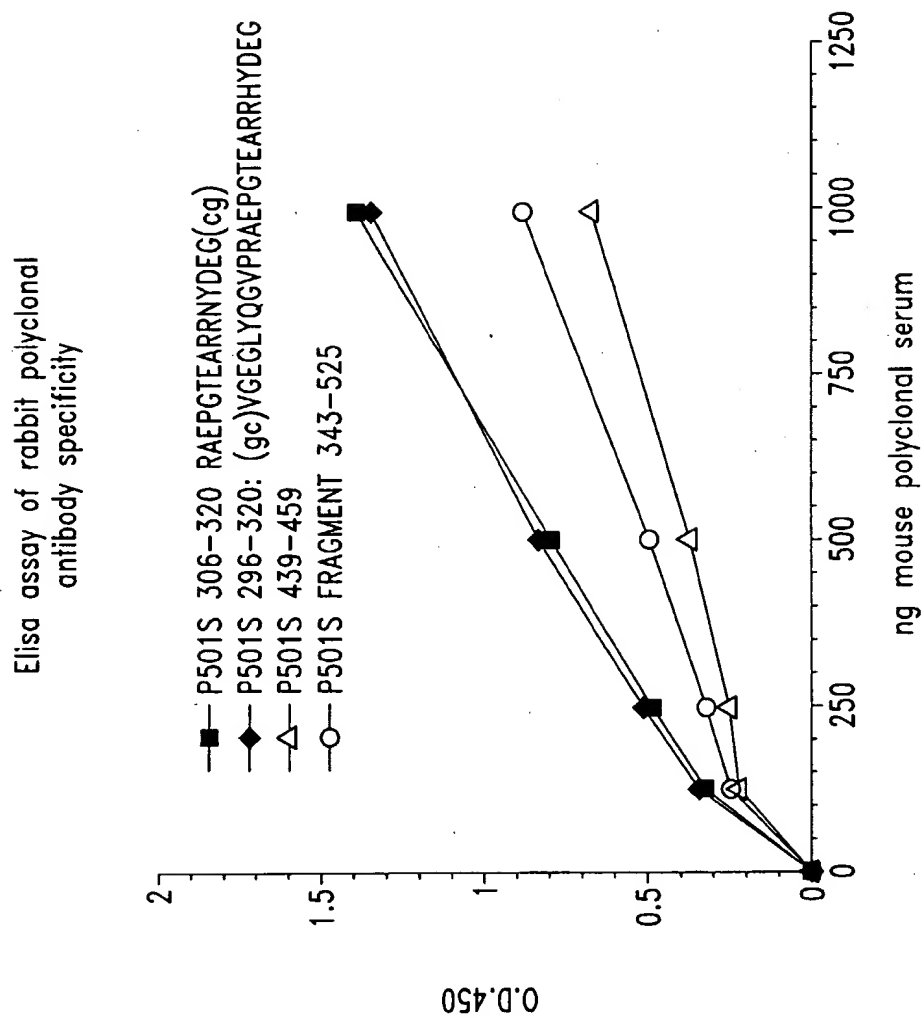
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caaggacaag gccaccaggt gcgggggccg aagcccacat gatccttact ctatgagcaa     180
aatcccctgt gggggcttct ccttgaagtc cgccancagg gctcagtctt tggacccang     240
caggtcatgg ggttgtngnc caactggggg ccncaacgca aaanggcnca gggcctcngn     300
cacccatccc angacgcggc tacactnctg gacctcccnc tccaccactt tcatgcgctg     360
ttcntacccg cgnatntgtc ccanctgttt cngtgccnac tccancttct nggacgtgcg     420
ctacatacgc ccggantcnc nctcccgctt tgtccctatc cacgtnccan caacaaattt     480
cnccntantg caccnattcc cacntttnnc agntttccnc nncgngcttc cttntaaaag     540
ggttgancccc cggaaaaatnc cccaaagggg ggggccngg tacccaactn ccccctnata    600
gctgaantcc ccatnaccnn gnctcnatgg anccntccnt tttaannacn ttctnaactt     660
gggaananccc ctcgnccntn cccccnttaa tcccnccttg cnangnncnt cccccnntcc    720
ncccnnntng gcntntnann caaaaaaggc ccnnnancaa tctcctnncn cctcanttcg     780
ccanccctcg aaatcggccn c                                               801
```

```
<210> 10
<211> 789
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(789)
<223> n = A,T,C or G

<400> 10
cagtctatnt ggccagtgtg gcagctttcc ctgtggctgc cggtgccaca tgcctgtccc      60
acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg gttcaccttc tcagccctgc     120
agatcctgcc ctacacactg gcctccctct accaccggga gaagcaggtg ttcctgccca     180
aataccgagg ggacactgga ggtgctagca gtgaggacag cctgatgacc agcttcctgc     240
caggccctaa gcctggagct cccttcccta atggacacgt gggtgctgga ggcagtggcc     300
tgctcccacc tccacccgcg ctctgcgggg cctctgcctg tgatgtctcc gtacgtgtgg     360
tggtgggtga gcccaccgan gccagggtgg ttccgggccg gggcatctgc ctggacctcg     420
ccatcctgga tagtgcttcc tgctgtccca ngtggcccca tccctgttta tgggctccat     480
tgtccagctc agccagtctg tcactgccta tatggtgtct gccgcaggcc tgggtctggt     540
cccatttact ttgctacaca ggtantattt gacaagaacg anttggccaa atactcagcg     600
ttaaaaaatt ccagcaacat tggggggtgga aggcctgcct cactgggtcc aactccccgc     660
tcctgttaac cccatggggc tgccggcttg ccgccaatt tctgttgctg ccaaantnat      720
gtggctctct gctgccacct gttgctggct gaagtgcnta cngcncanct nggggggtng     780
ggngttccc                                                            789
```

```
<210> 11
<211> 772
```

```
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(772)
<223> n = A,T,C or G

<400> 11
cccaccctac ccaaatatta gacaccaaca cagaaaagct agcaatggat tcccttctac        60
tttgttaaat aaataagtta aatatttaaa tgcctgtgtc tctgtgatgg caacagaagg       120
accaacaggc cacatcctga taaaaggtaa gagggggtg gatcagcaaa aagacagtgc        180
tgtgggctga ggggacctgg ttcttgtgtg ttgcccctca ggactcttcc cctacaaata       240
actttcatat gttcaaatcc catggaggag tgtttcatcc tagaaactcc catgcaagag       300
ctacattaaa cgaagctgca ggttaagggg cttanagatg ggaaaccagg tgactgagtt       360
tattcagctc ccaaaaaccc ttctctaggt gtgtctcaac taggaggcta gctgttaacc       420
ctgagcctgg gtaatccacc tgcagagtcc ccgcattcca gtgcatggaa cccttctggc       480
ctccctgtat aagtccagac tgaaaccccc ttggaaggnc tccagtcagg cagccctana       540
aactggggaa aaaagaaaag gacgccccan cccccagctg tgcanctacg cacctcaaca       600
gcacagggtg gcagcaaaaa aaccacttta ctttggcaca aacaaaaact nggggggggca      660
accccggcac cccnangggg gttaacagga ancngggnaa cntggaaccc aattnaggca       720
ggcccnccac cccnaatntt gctgggaaat ttttcctccc ctaaattntt tc              772

<210> 12
<211> 751
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(751)
<223> n = A,T,C or G

<400> 12
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa        60
agctgattga agcaaccctc tactttttgg tcgtgagcct tttgcttggt gcaggtttca       120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg       180
aagtanggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc       240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca       300
ggcactacca gcaacgtcag ggaagtgctc agccattgtg gtgtacacca aggcgaccac       360
agcagctgcn acctcagcaa tgaagatgan gaggangatg aagaagaacg tcncgagggc       420
acacttgctc tcagtcttan caccatanca gcccntgaaa accaananca aagaccacna       480
cnccggctgc gatgaagaaa tnaccccncg ttgacaaact tgcatggcac tggganccac       540
agtggcccna aaaatcttca aaaaggatgc cccatcnatt gaccccccaa atgcccactg       600
ccaacagggg ctgccccacn cncnnaacga tganccnatt gnacaagatc tncntggtct       660
tnatnaacnt gaaccctgcn tngtggctcc tgttcaggnc cnnggcctga cttctnaann       720
aangaactcn gaagnccca cnggananc g                                      751

<210> 13
<211> 729
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(729)
<223> n = A,T,C or G
```

```
    <400> 13
gagccaggcg tccctctgcc tgcccactca gtggcaacac ccgggagctg ttttgtcctt      60
tgtggancct cagcagtncc ctctttcaga actcantgcc aagancccctg aacaggagcc     120
accatgcagt gcttcagctt cattaagacc atgatgatcc tcttcaattt gctcatcttt     180
ctgtgtggtg cagccctgtt ggcagtgggc atctgggtgt caatcgatgg ggcatccttt     240
ctgaagatct tcgggccact gtcgtccagt gccatgcagt ttgtcaacgt gggctacttc     300
ctcatcgcag ccggcgttgt ggtcttagct ctaggtttcc tgggctgcta tggtgctaag     360
actgagagca agtgtgccct cgtgacgttc ttcttcatcc tcctcctcat cttcattgct     420
gaggttgcaa tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt     480
tgctggtaat gcctgccatc aanaaaagat tatgggttcc caggaanact tcactcaagt     540
gttggaacac caccatgaaa gggctcaagt gctgtggctt cnnccaacta tacggatttt     600
gaagantcac ctacttcaaa gaaaanagtg cctttcccccc atttctgttg caattgacaa     660
acgtccccaa cacagccaat tgaaaacctg cacccaacccc aaangggtcc ccaaccanaa     720
attnaaggg                                                              729

    <210> 14
    <211> 816
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(816)
    <223> n = A,T,C or G

    <400> 14
tgctcttcct caaagttgtt cttgttgcca taacaaccac cataggtaaa gcgggcgcag      60
tgttcgctga aggggttgta gtaccagcgc gggatgctct ccttgcagag tcctgtgtct     120
ggcaggtcca cgcagtgccc tttgtcactg gggaaatgga tgcgctggag ctcgtcaaag     180
ccactcgtgt attttttcaca ggcagcctcg tccgacgcgt cggggcagtt ggggggtgtct    240
tcacactcca ggaaactgtc natgcagcag ccattgctgc agcggaactg ggtgggctga     300
cangtgccag agcacactgg atggcgcctt ccatgnnan gggccctgng ggaaagtccc      360
tganccccan anctgcctct caaangcccc accttgcaca ccccgacagg ctagaatgga     420
atcttcttcc cgaaaggtag ttnttcttgt tgcccaancc anccccntaa acaaactctt      480
gcanatctgc tccgnggggg tcntantacc ancgtgggaa aagaacccca ggcngcgaac     540
caancttgtt tggatncgaa gcnataatct nctnttctgc ttggtggaca gcaccantna     600
ctgtnnanct ttagnccntg gtcctcntgg gttgnncttg aacctaatcn ccnntcaact     660
gggacaaggt aantngccnt cctttnaatt cccnancntn ccccctggtt tggggtttttn    720
cncnctccta ccccagaaan nccgtgttcc cccccaacta ggggccnaaa ccnnttnttc     780
cacaaccctn ccccacccac gggttcngnt ggttng                               816

    <210> 15
    <211> 783
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(783)
    <223> n = A,T,C or G

    <400> 15
ccaaggcctg ggcaggcata nacttgaagg tacaaccccca ggaacccctg gtgctgaagg      60
atgtggaaaa cacagattgg cgcctactgc ggggtgacac ggatgtcagg gtagagagga     120
aagacccaaa ccaggtggaa ctgtggggac tcaaggaang cacctacctg ttccagctga     180
cagtgactag ctcagaccac ccagaggaca cggccaacgt cacagtcact gtgctgtcca     240
ccaagcagac agaagactac tgcctcgcat ccaacaangt gggtcgctgc cggggctctt     300
tcccacgctg gtactatgac cccacggagc agatctgcaa gagtttcgtt tatggaggct     360
```

```
gcttgggcaa caagaacaac taccttcggg aagaagagtg cattctancc tgtcnggtg      420
tgcaaggtgg gcctttgana ngcanctctg gggctcangc gactttcccc cagggcccct     480
ccatggaaag gcgccatcca ntgttctctg gcacctgtca gcccacccag ttccgctgca     540
ncaatggctg ctgcatcnac antttcctng aattgtgaca acacccccca ntgcccccaa     600
ccctcccaac aaagcttccc tgttnaaaaa tacnccattt ggcttttnac aaacncccgg     660
cncctccntt ttccccnntn aacaaagggc nctngcnttt gaactgcccn aacccnggaa     720
tctnccnngg aaaaantncc ccccctggtt cctnnaancc cctccncnaa anctnccccc     780
ccc                                                                  783
```

        <210> 16
        <211> 801
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(801)
        <223> n = A,T,C or G

        <400> 16
```
gccccaattc cagctgccac accacccacg gtgactgcat tagttcggat gtcatacaaa      60
agctgattga agcaaccctc tacttttttgg tcgtgagcct tttgcttggt gcaggtttca    120
ttggctgtgt tggtgacgtt gtcattgcaa cagaatgggg gaaaggcact gttctctttg    180
aagtagggtg agtcctcaaa atccgtatag ttggtgaagc cacagcactt gagccctttc    240
atggtggtgt tccacacttg agtgaagtct tcctgggaac cataatcttt cttgatggca    300
ggcactacca gcaacgtcag gaagtgctca gccattgtgg tgtacaccaa ggcgaccaca    360
gcagctgcaa cctcagcaat gaagatgagg aggaggatga agaagaacgt cncgagggca    420
cacttgctct ccgtcttagc accatagcag cccangaaac caagagcaaa gaccacaacg    480
ccngctgcga atgaaagaaa ntacccacgt tgacaaactg catggccact ggacgacagt    540
tggcccgaan atcttcagaa aagggatgcc ccatcgattg aacacccana tgcccactgc    600
cnacagggct gcnccncncn gaaagaatga gccattgaag aaggatcntc ntggtcttaa    660
tgaactgaaa cntgcatgg tggcccctgt tcagggctct tggcagtgaa ttctganaaa     720
aaggaacngc ntnagcccccc ccaaangana aaacacccccc gggtgttgcc ctgaattggc   780
ggccaaggan ccctgccccn g                                               801
```

        <210> 17
        <211> 740
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(740)
        <223> n = A,T,C or G

        <400> 17
```
gtgagagcca ggcgtccctc tgcctgccca ctcagtggca acacccggga gctgttttgt      60
cctttgtgga gcctcagcag ttccctcttt cagaactcac tgccaagagc cctgaacagg    120
agccaccatg cagtgcttca gcttcattaa gaccatgatg atcctcttca atttgctcat    180
ctttctgtgt ggtgcagccc tgttggcagt gggcatctgg gtgtcaatcg atggggcatc    240
ctttctgaag atcttcgggc cactgtcgtc cagtgccatg cagtttgtca acgtgggcta    300
cttcctcatc gcagccggcg ttgtggtctt tgctcttggt ttcctgggct gctatggtgc    360
taagacggag agcaagtgtg ccctcgtgac gttcttcttc atcctcctcc tcatcttcat    420
tgctgaagtt gcagctgctg tggtcgcctt ggtgtacacc acaatggctg aaccattcct    480
gacgttgctg gtantgcctg ccatcaanaa agattatggg ttcccaggaa aaattcactc    540
aantntggaa caccnccatg aaaagggctc caatttctgn tggcttcccc aactataccg    600
gaattttgaa agantcnccc tacttccaaa aaaaaanant tgcctttncc cccnttctgt    660
tgcaatgaaa acntcccaan acngccaatn aaaacctgcc cnnncaaaaa ggntcncaaa    720
```

caaaaaaant nnaagggttn   740

```
        <210> 18
        <211> 802
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(802)
        <223> n = A,T,C or G

        <400> 18
ccgctggttg cgctggtcca gngnagccac gaagcacgtc agcatacaca gcctcaatca       60
caaggtcttc cagctgccgc acattacgca gggcaagagc ctccagcaac actgcatatg      120
ggatacactt tactttagca gccagggtga caactgagag gtgtcgaagc ttattcttct      180
gagcctctgt tagtggagga agattccggg cttcagctaa gtagtcagcg tatgtcccat      240
aagcaaacac tgtgagcagc cggaaggtag aggcaaagtc actctcagcc agctctctaa      300
cattgggcat gtccagcagt tctccaaaca cgtagacacc agnggcctcc agcacctgat      360
ggatgagtgt ggccagcgct gcccccttgg ccgacttggc taggagcaga aattgctcct      420
ggttctgccc tgtcaccttc acttccgcac tcatcactgc actgagtgtg ggggacttgg      480
gctcaggatg tccagagacg tggttccgcc ccctcnctta atgacaccgn ccanncaacc      540
gtcggctccc gccgantgng ttcgtcgtnc ctgggtcagg gtctgctggc cnctacttgc      600
aancttcgtc nggcccatgg aattcaccnc accggaactn gtangatcca ctnnttctat      660
aaccggncgc caccgcnnnt ggaactccac tcttnttncc tttacttgag ggttaaggtc      720
acccttnncg ttaccttggt ccaaaccntn ccntgtgtcg anatngtnaa tcnggnccna      780
tnccanccnc atangaagcc ng                                                802

        <210> 19
        <211> 731
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(731)
        <223> n = A,T,C or G

        <400> 19
cnaagcttcc aggtnacggg ccgcnaancc tgacccnagg tancanaang cagncngcgg       60
gagcccaccg tcacgngggn gngtctttat nggaggggge ggagccacat cnctggacnt      120
cntgaccccca actccccncc ncncantgca gtgatgagtg cagaactgaa ggtnacgtgg      180
caggaaccaa gancaaannc tgctccnntc caagtcggcn naggggggcgg ggctggccac      240
gcncatccnt cnagtgctgn aaagcccccnn cctgtctact tgtttggaga acngcnnnga      300
catgcccagn gttanataac nggcngagag tnantttgcc tctcccttcc ggctgcgcan      360
cgngtntgct tagnggacat aacctgacta cttaactgaa cccnngaatc tnccncccct      420
ccactaagct cagaacaaaa aacttcgaca ccactcantt gtcacctgnc tgctcaagta      480
aagtgtaccc catncccaat gtntgctnga ngctctgncc tgcnttangt tcggtcctgg      540
gaagacctat caattnaagc tatgtttctg actgcctctt gctccctgna acaancnacc      600
cnncnntcca aggggggggnc ggccccccaat cccccnaacc ntnaattnan tttancccccn      660
ccccnggcc cggcctttta cnancntcnn nnacngggna aaaccnnngc tttncccaac      720
nnaatccncc t                                                            731

        <210> 20
        <211> 754
        <212> DNA
        <213> Homo sapien
```

```
        <220>
        <221> misc_feature
        <222> (1)...(754)
        <223> n = A,T,C or G

        <400> 20
tttttttttt tttttttttt taaaaacccc ctccattnaa tgnaaacttc cgaaattgtc      60
caacccccctc ntccaaatnn ccntttccgg gnggggggttc caaacccaan ttannttttgg    120
annttaaatt aaatnttnnt tggnggnnna anccnaatgt nangaaagtt naacccanta      180
tnancttnaa tncctggaaa ccngtngntt ccaaaaatnt ttaaccctta antccctccg      240
aaatngttna nggaaaaccc aanttctcnt aaggttgttt gaaggntnaa tnaaaanccc      300
nnccaattgt ttttngccac gcctgaatta attggnttcc gntgttttcc nttaaaanaa      360
ggnnanccccc ggttantnaa tccccccnnc cccaattata ccganttttt ttngaattgg     420
ganccccncgg gaattaacgg ggnnnntccc tnttgggggg cnggnnccccc ccccntcggg    480
ggttngggnc aggncnnaat tgtttaaggg tccgaaaaat ccctccnaga aaaaaanctc       540
ccaggntgag nntngggttt nccccccccc canggcccct ctcgnanagt tggggtttgg      600
ggggcctggg atttttntttc ccctnttncc tccccccccc ccngggganag aggttngngt     660
tttgntcnnc ggcccnccn aaganctttn ccganttnan ttaaatccnt gcctnggcga      720
agtccnttgn agggntaaan ggcccctnn cggg                                   754
```

```
            <210> 21
            <211> 755
            <212> DNA
            <213> Homo sapien

            <220>
            <221> misc_feature
            <222> (1)...(755)
            <223> n = A,T,C or G

            <400> 21
atcancccat gaccccnaac nnggaccnc tcanccggnc nnncnaccnc cggccnatca      60
nngtnagnnc actncnnttn natcacnccc cnccnactac gcccncnanc cnacgcncta      120
nncanatncc actgannngcg cgangtngan ngagaaanct nataccanag ncaccanacn     180
ccagctgtcc nanaangcct nnnatacngg nnnatccaat ntgnancctc cnaagtattn      240
nncnncanat gattttcctn anccgattac ccntncccccc tanccctcc cccccaacna     300
cgaaggcnct ggnccnaagg nngcgncncc ccgctagntc cccnncaagt cncncnccta      360
aactcanccn nattacncgc ttcntgagta tcactccccg aatctcaccc tactcaactc     420
aaaaaanatcn gatacaaaat aatncaagcc tgnttatnac actntgactg ggtctctatt    480
ttagnggtcc ntnaancntc ctaatacttc cagtctncct tcnccaattt ccnaanggct     540
ctttcngaca gcatnttttg gttcccnntt gggttcttan ngaattgccc ttcntngaac     600
gggctcntct tttccttcgg ttanccctggn ttcnnccggc cagttattat ttcccnttttt    660
aaattcntnc cntttantttt tggcnttcna aaccccccggc cttgaaaacg gcccccctggt   720
aaaaggttgt tttganaaaa tttttgtttt gttcc                                 755
```

```
            <210> 22
            <211> 849
            <212> DNA
            <213> Homo sapien

            <220>
            <221> misc_feature
            <222> (1)...(849)
            <223> n = A,T,C or G

            <400> 22
tttttttttt tttttangtg tngtcgtgca ggtagaggct tactacaant gtgaanacgt      60
acgctnggan taangcgacc cganttctag gannncnccct aaaatcanac tgtgaagatn     120
```

```
atcctgnnna cggaanggtc accggnngat nntgctaggg tgnccnctcc cannncnttn    180
cataactcng nggccctgcc caccaccttc ggcggcccng ngnccgggcc cgggtcattn    240
gnnttaaccn cactnngcna ncggtttccn ncccnncng accnggcga tccgggggtnc    300
tctgtcttcc cctgnagncn anaaantggg ccncggnccc ctttacccct nnacaagcca    360
cngccntcta nccncngccc ccctccant nngggggact gccnanngct ccgttnctng    420
nnaccccnnn gggtncctcg gttgtcgant cnaccgnang ccanggattc cnaaggaagg    480
tgcgttnttg gccctaccc ttcgctncgg nncacccttc ccgacnanga nccgctcccg    540
cncnncgnng cctcncctcg caacaccgc nctcntcngt ncggnnnccc ccccacccgc    600
nccctcncnc ngncgnancn ctccnccncc gtctcannca ccaccccgcc ccgccaggcc    660
ntcanccacn ggnngacnng nagcncnntc gcnccgcgcn gcgncncccct cgccncngaa   720
ctncntcngg ccantnncgc tcaanccnna cnaaacgccg ctgcgcggcc cgnagcgncc    780
ncctccncga gtcctcccgn cttccnaccc angnnttccn cgaggacacn nnaccccgcc    840
nncangcgg                                                           849
```

```
    <210> 23
    <211> 872
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(872)
    <223> n = A,T,C or G

    <400> 23
gcgcaaacta tacttcgctc gnactcgtgc gcctcgctnc tcttttcctc cgcaaccatg    60
tctgacnanc ccgattnggc ngatatcnan aagntcganc agtccaaact gantaacaca    120
cacacncnan aganaaatcc nctgccttcc anagtanacn attgaacnng agaaccangc    180
nggcgaatcg taatnaggcg tgcgccgcca atntgtcncc gtttattntn ccagcntcnc    240
ctnccnaccc tacntcttcn nagctgtcnn acccctngtn cgnaccccc naggtcggga    300
tcgggtttnn nntgaccgng cnnccctcc ccccntccat nacgancnc ccgcaccacc    360
nanngcncgc nccccgnnct cttcgccncc ctgtcctntn ccctgtngc ctggcncgn    420
accgcattga ccctcgccnn ctncnngaaa ncgnanacgt ccgggttgnn annancgctg    480
tgggnnngcg tctgcnccgc gttccttccn ncnncttcca ccatcttcnt tacngggtct    540
ccncgccntc tcnnncacnc cctgggacgc tntcctntgc cccccttnac tccccccctt    600
cgncgtgncc cgnccccacc ntcatttnca nacgntcttc acaannncct ggntnnctcc    660
cnancngncn gtcanccnag ggaagggngg ggnnccnntg nttgacgttg nggngangtc    720
cgaanantcc tcnccntcan cnctacccct cgggcgnnct ctcngttncc aacttancaa    780
ntctcccccg ngngcncntc tcagcctcnc ccnccccnct ctctgcantg tnctctgctc    840
tnaccnntac gantnttcgn cnccctcttt cc                                  872
```

```
    <210> 24
    <211> 815
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(815)
    <223> n = A,T,C or G

    <400> 24
gcatgcaagc ttgagtattc tatagngtca cctaaatanc ttggcntaat catggtcnta    60
nctgncttcc tgtgtcaaat gtatacnaan tanatatgaa tctnatntga caaganngta    120
tcntncatta gtaacaantg tnntgtccat cctgtcngan canattccca tnnattncgn    180
cgcattcncn gcncantatn taatnggnaa ntcnnntnnn ncaccnncat ctatcntncc    240
gcnccctgac tggnagagat ggatnanttc tnntntgacc nacatgttca tcttggattn    300
aananccccc cgcngnccac cggttngnng cnagccnntc ccaagacctc ctgtggaggt    360
```

```
aacctgcgtc aganncatca aacntgggaa acccgcnncc angtnnaagt ngnnncanan    420
gatcccgtcc aggnttnacc atcccttcnc agcgccccct ttngtgcctt anagngnagc    480
gtgtccnanc cnctcaacat ganacgcgcc agnccanccg caattnggca caatgtcgnc    540
gaacccccta gggggantna tncaaanccc caggattgtc cncncangaa atcccncanc    600
cccncccctac ccnnctttgg gacngtgacc aantcccgga gtnccagtcc ggccngnctc    660
ccccaccggt nnccntgggg gggtgaanct cngnntcanc cngncgaggn ntcgnaagga    720
accggnccth ggncgaanng ancnntcnga agngccncnt cgtataaccc cccctcncca    780
nccnacngnt agntcccccc cngggtncgg aangg                              815
```

        <210> 25
        <211> 775
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(775)
        <223> n = A,T,C or G

        <400> 25
```
ccgagatgtc tcgctccgtg gccttagctg tgctcgcgct actctctctt tctggcctgg     60
aggctatcca gcgtactcca aagattcagg tttactcacg tcatccagca gagaatggaa    120
agtcaaattt cctgaattgc tatgtgtctg ggtttcatcc atccgacatt gaanttgact    180
tactgaagaa tgganagaga attgaaaaag tggagcattc agacttgtct ttcagcaagg    240
actggtcttt ctatctcntg tactacactg aattcacccc cactgaaaaa gatgagtatg    300
cctgccgtgt gaaccatgtg actttgtcac agcccaagat agttaagtgg gatcgagaca    360
tgtaagcagn cnncatggaa gtttgaagat gccgcatttg gattggatga attccaaatt    420
ctgcttgctt gcnttttaat antgatatgc ntatacaccc taccctttat gnccccaaat    480
tgtaggggtt acatnantgt tcncntggga catgatcttc ctttataant ccnccnttcg    540
aattgcccgt cncccngttn ngaatgtttc cnnaaccacg gttggctccc ccaggtcncc    600
tcttacggaa gggcctgggc cncttttcaa ggttggggga accnaaaatt tcncttntgc    660
ccncccncca cnntcttgng nncncanttt ggaacccttc cnattcccct tggcctcnna    720
nccttnncta anaaaacttn aaancgtngc naaanntttn acttcccccc ttacc         775
```

        <210> 26
        <211> 820
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(820)
        <223> n = A,T,C or G

        <400> 26
```
anattantac agtgtaatct tttcccagag gtgtgtanag ggaacggggc ctagaggcat     60
cccanagata ncttatanca acagtgcttt gaccaagagc tgctgggcac atttcctgca    120
gaaaaggtgg cggtccccat cactcctcct ctcccatagc catcccagag gggtgagtag    180
ccatcangcc ttcggtggga gggagtcang gaaacaacan accacagagc anacagacca    240
ntgatgacca tgggcgggag cgagcctctt ccctgnaccg gggtggcana nganagccta    300
nctgaggggt cacactataa acgttaacga ccnagatnan cacctgcttc aagtgcaccc    360
ttcctacctg acnaccagng accnnnaact gcngcctggg gacagcnctg ggancagcta    420
acnnagcact cacctgcccc cccatggccg tncgcntccc tggtcctgnc aagggaagct    480
ccctgttgga attncgggga naccaaggga ncccccctcct ccanctgtga aggaaaaann    540
gatggaattt tnccccttccg gccnntcccc tcttccttta cacgccccct nntactcntc    600
tccctctntt ntcctgncnc acttttnacc ccnnnatttc ccttnattga tcggannctn    660
ganattccac tnncgcctnc cntcnatcng naanacnaaa nactntctna cccngggggat    720
gggnnccccg ntcatcctct ctttttcnct accnccnntt ctttgcctct ccttngatca    780
```

```
tccaaccntc gntggccntn cccccccnnn tcctttnccc                              820
```

```
        <210> 27
        <211> 818
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(818)
        <223> n = A,T,C or G

        <400> 27
tctgggtgat ggcctcttcc tcctcaggga cctctgactg ctctgggcca aagaatctct       60
tgtttcttct ccgagcccca ggcagcggtg attcagccct gcccaacctg attctgatga      120
ctgcggatgc tgtgacggac ccaaggggca aatagggtcc cagggtccag ggaggggcgc      180
ctgctgagca cttccgcccc tcaccctgcc cagcccctgc catgagctct gggctgggtc      240
tccgcctcca gggttctgct cttccangca ngccancaag tggcgctggg ccacactggc      300
ttcttcctgc cccntccctg gctctgantc tctgtcttcc tgtcctgtgc angcnccttg      360
gatctcagtt tccctcnctc anngaactct gtttctgann tcttcantta actntgantt      420
tatnaccnan tggnctgtnc tgtcnnactt taatgggccn gaccggctaa tccctccctc      480
nctcccttcc anttcnnnna accngcttnc cntcntctcc ccntacccg ccngggaanc       540
ctcctttgcc ctnaccangg gccnnnaccg cccntnnctn ggggggcnng gtnnctncnc      600
ctgntnnccc cnctcncnnt tncctcgtcc cnncnncgcn nngcannttc ncgtcccnn       660
tnnctcttcn ngtntcgnaa ngntcncntn tnnnnngncn ngntnntncn tccctctcnc      720
cnnntgnang tnnttnnnnc ncngnncccc nnnncnnnnn nggnnntnnn tctncncngc      780
cccnnccccc ngnattaagg cctccnntct ccggccnc                              818
```

```
        <210> 28
        <211> 731
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(731)
        <223> n = A,T,C or G

        <400> 28
aggaagggcg gagggatatt gtangggatt gagggatagg agnataangg gggaggtgtg       60
tcccaacatg anggtgnngt tctcttttga angagggttg ngtttttann ccnggtgggt      120
gattnaaccc cattgtatgg agnnaaaggn tttnagggat ttttcggctc ttatcagtat      180
ntanattcct gtnaatcgga aaatnatntt tcnncnggaa aatnttgctc ccatccgnaa      240
attnctcccg ggtagtgcat nttnggggn cngccangtt tcccaggctg ctanaatcgt      300
actaaagntt naagtgggan tncaaatgaa aacctnncac agagnatccn tacccgactg      360
tnnnttncct tcgccctntg actctgcnng agcccaatac ccnngngnat gtcncccngn      420
nnngcgncnc tgaaannnnc tcgnggctnn gancatcang gggtttcgca tcaaaaagcnn     480
cgtttcncat naaggcactt tngcctcatc caaccnctng ccctcnncca tttngccgtc      540
nggttcncct acgctnnntg cncctnnntn ganattttnc ccgcctgggg naancctcct      600
gnaatgggta gggncttntc ttttnaccnn gnggtntact aatcnnctnc acgcntnctt      660
tctcnacccc cccccttttt caatcccanc ggcnaatggg gtctcccnn cgangggggg      720
nnncccannc c                                                           731
```

```
        <210> 29
        <211> 822
        <212> DNA
        <213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(822)
<223> n = A,T,C or G

<400> 29
actagtccag tgtggtggaa ttccattgtg ttggggncnc ttctatgant antnttagat      60
cgctcanacc tcacancctc ccnacnangc ctataangaa nannaataga nctgtncnnt     120
atntntacnc tcatanncct cnnnacccac tccctcttaa cccntactgt gcctatngcn     180
tnnctantct ntgccgcctn cnanccaccn gtgggccnac cncnngnatt ctcnatctcc     240
tcnccatntn gcctananta ngtncatacc ctatacctac nccaatgcta nnnctaancn     300
tccatnantt annntaacta ccactgacnt ngactttcnc atnanctcct aatttgaatc     360
tactctgact cccacngcct annnattagc ancntccccc nacnatntct caaccaaatc     420
ntcaacaacc tatctcanctg ttcnccaacc nttncctccg atccccnnac aacccccctc     480
ccaaataccc nccacctgac ncctaacccn caccatcccg gcaagccnan ggncatttan     540
ccactggaat cacnatngga naaaaaaaac ccnaactctc tancncnnat ctccctaana     600
aatnctcctn naatttactn ncantnccat caancccacn tgaaacnnaa ccccctgtttt     660
tanatcccctt ctttcgaaaa ccnacccttt annncccaac ctttngggcc ccccncctnc     720
ccnaatgaag gncncccaat cnangaaacg nccntgaaaa ancnaggcna anannntccg     780
canatcctat cccttanttn ggggnccctt ncccngggcc cc                       822
```

```
<210> 30
<211> 787
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(787)
<223> n = A,T,C or G

<400> 30
cggccgcctg ctctggcaca tgcctcctga atggcatcaa aagtgatgga ctgcccattg      60
ctagagaaga ccttctctcc tactgtcatt atggagccct gcagactgag ggctcccctt     120
gtctgcagga tttgatgtct gaagtcgtgg agtgtggctt ggagctcctc atctacatna     180
gctggaagcc ctggagggcc tctctcgcca gcctcccccct tctctccacg ctctccangg     240
acaccagggg ctccaggcag cccattattc ccagnangac atggtgtttc tccacgcgga     300
cccatggggc ctgnaaggcc agggtctcct ttgacaccat ctctcccgtc ctgcctggca     360
ggccgtggga tccactantt ctanaacggn cgccaccncg gtgggagctc cagcttttgt     420
tcccnttaat gaaggttaat tgcncgcttg gcgtaatcat nggtcanaac tntttcctgt     480
gtgaaattgt ttntcccctc ncnattccnc ncnacatacn aacccggaan cataaagtgt     540
taaagcctgg gggtngcctn nngaatnaac tnaactcaat taattgcgtt ggctcatggc     600
ccgctttccn ttcnggaaaa ctgtcntccc ctgcnttnnt gaatcggcca cccccnggg     660
aaaagcggtt tgcnttttng ggggntcctt ccncttcccc cctcnctaan ccctncgcct     720
cggtcgttnc nggtngcggg gaangggnat nnnctcccnc naagggggng agnnngntat     780
ccccaaa                                                                787
```

```
<210> 31
<211> 799
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(799)
<223> n = A,T,C or G

<400> 31
```

15

```
tttttttttt ttttttttggc gatgctactg tttaattgca ggaggtgggg gtgtgtgtac        60
catgtaccag ggctattaga agcaagaagg aaggagggag ggcagagcgc cctgctgagc       120
aacaaaggac tcctgcagcc ttctctgtct gtctcttggc gcaggcacat ggggaggcct       180
cccgcagggt gggggccacc agtccagggg tgggagcact acangggtg ggagtgggtg       240
gtggctggtn cnaatggcct gncacanatc cctacgattc ttgacacctg gatttcacca       300
ggggaccttc tgttctccca nggnaacttc ntnnatctcn aaagaacaca actgtttctt       360
cngcanttct ggctgttcat ggaaagcaca ggtgtccnat ttnggctggg acttggtaca       420
tatggttccg gcccacctct cccntcnaan aagtaattca cccccccccn ccntctnttg       480
cctgggccct taantaccca caccggaact canttantta ttcatcttng gntgggcttg       540
ntnatcnccn cctgaangcg ccaagttgaa aggccacgcc gtnccnctc cccatagnan       600
nttttnncnt canctaatgc cccccnggc aacnatccaa tccccccccn tgggggcccc       660
agcccanggc ccccgnctcg ggnnccngn cncgnantcc ccaggntctc ccantcngnc       720
ccnnngcncc cccgcacgca gaacanaagg ntngagccnc cgcannnnnn nggtnncnac       780
ctcgcccccc ccnncgnng                                                     799
```

```
        <210> 32
        <211> 789
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(789)
        <223> n = A,T,C or G

        <400> 32
tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt        60
ttttnccnag ggcaggttta ttgacaacct cncgggacac aancaggctg gggacaggac       120
ggcaacaggc tccggcggcg gcggcggcgg ccctacctgc ggtaccaaat ntgcagcctc       180
cgctcccgct tgatnttcct ctgcagctgc aggatgccnt aaaacagggc ctcggccntn       240
ggtgggcacc ctgggatttn aatttccacg ggcacaatgc ggtcgcancc cctcaccacc       300
nattaggaat agtggtntta cccnccnccg ttggcncact ccccntggaa accacttntc       360
gcggctccgg catctggtct taaaccttgc aaacnctggg gccctctttt tggttantnt       420
nccngccaca atcatnactc agactggcnc gggctggccc caaaaaancn ccccaaaacc       480
ggnccatgtc ttnncggggt tgctgcatn tncatcacct cccgggcnca ncaggncaac       540
ccaaaagttc ttgnggcccn caaaaaanct ccgggggggnc ccagtttcaa caaagtcatc       600
ccccttggcc cccaaatcct ccccccgntt nctgggtttg ggaacccacg cctctnnctt       660
tggnnggcaa gntggntccc ccttcgggcc cccggtgggc ccnnctctaa ngaaaacncc       720
ntcctnnnca ccatcccccc nngnnacgnc tancaangna tccctttttt tanaaacggg       780
cccccncg                                                                 789
```

```
        <210> 33
        <211> 793
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(793)
        <223> n = A,T,C or G

        <400> 33
gacagaacat gttggatggt ggagcacctt tctatacgac ttacaggaca gcagatgggg        60
aattcatggc tgttggagca atanaacccc agttctacga gctgctgatc aaaggacttg       120
gactaaagtc tgatgaactt cccaatcaga tgagcatgga tgattggcca gaaatgaana       180
agaagtttgc agatgtattt gcaaagaaga cgaaggcaga gtggtgtcaa atctttgacg       240
gcacagatgc ctgtgtgact ccggttctga cttttgagga ggttgttcat catgatcaca       300
acaangaacg gggctcgttt atcaccantg aggagcagga cgtgagcccc cgccctgcac       360
```

```
ctctgctgtt aaacacccca gccatccctt ctttcaaaag ggatccacta cttctagagc      420
ggncgccacc gcggtggagc tccagctttt gttcccttta gtgagggtta attgcgcgct      480
tggcgtaatc atggtcatan ctgtttcctg tgtgaaattg ttatccgctc acaattccac      540
acaacatacg anccggaagc atnaaatttt aaagcctggn ggtngcctaa tgantgaact      600
nactcacatt aattggcttt gcgctcactg cccgctttcc agtccggaaa acctgtcctt      660
gccagctgcc nttaatgaat cnggccaccc cccgggggaaa aggcngtttg cttnttgggg      720
cgcncttccc gctttctcgc ttcctgaant ccttcccccc ggtctttcgg cttgcggcna      780
acggtatcna cct                                                          793
```

        <210> 34
        <211> 756
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(756)
        <223> n = A,T,C or G

        <400> 34
```
gccgcgaccg gcatgtacga gcaactcaag ggcgagtgga accgtaaaag ccccaatctt       60
ancaagtgcg gggaanagct gggtcgactc aagctagttc ttctggagct caacttcttg      120
ccaaccacag ggaccaagct gaccaaacag cagctaattc tggcccgtga catactggag      180
atcggggccc aatggagcat cctacgcaan gacatcccct ccttcgagcg ctacatggcc      240
cagctcaaat gctactactt tgattacaan gagcagctcc ccgagtcagc ctatatgcac      300
cagctcttgg gcctcaacct cctcttcctg ctgtcccaga accgggtggc tgantnccac      360
acgganttgg ancggctgcc tgcccaanga catacanacc aatgtctaca tcnaccacca      420
gtgtcctgga gcaatactga tgganggcag ctaccncaaa gtnttcctgg ccnagggtaa      480
catcccccgc cgagagctac accttcttca ttgacatcct gctcgacact atcagggatg      540
aaaatcgcng ggttgctcca gaaaggctnc aanaanatcc ttttcnctga aggcccccgg      600
atncnctagt nctagaatcg gcccgccatc gcggtgganc ctccaacctt tcgttnccct      660
ttactgaggg ttnattgccg cccttggcgt tatcatggtc acnccngttn cctgtgttga      720
aattnttaac cccccacaat tccacgccna cattng                                756
```

        <210> 35
        <211> 834
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(834)
        <223> n = A,T,C or G

        <400> 35
```
ggggatctct anatcnacct gnatgcatgg ttgtcggtgt ggtcgctgtc gatgaanatg       60
aacaggatct tgcccttgaa gctctcggct gctgtntta agttgctcag tctgccgtca      120
tagtcagaca cnctcttggg caaaaaacan caggatntga gtcttgattt cacctccaat      180
aatcttcngg gctgtctgct cggtgaactc gatgacnang ggcagctggt tgtgtntgat      240
aaantccanc angttctcct tggtgacctc cccttcaaag ttgttccggc cttcatcaaa      300
cttctnnaan angannancc canctttgtc gagctggnat ttgganaaca cgtcactgtt      360
ggaaactgat cccaaatggt atgtcatcca tcgcctctgc tgcctgcaaa aaacttgctt      420
ggcncaaatc cgactccccn tccttgaaag aagccatca caccccctc cctggactcc      480
nncaangact ctnccgctnc cccntccnng cagggttggt ggcannccgg gcccntcgcgc    540
ttcttcagcc agttcacnat nttcatcagc ccctctgcca gctgttntat tccttggggg    600
ggaanccgtc tctcccttcc tgaannaact ttgaccgtng aatagccgc gcntcncnt       660
acntnctggg ccgggttcaa antccctccn ttgncnntcn cctcgggcca ttctggattt    720
nccnaacttt ttccttcccc cncccncgg ngtttggntt tttcatnggg ccccaactct     780
```

```
gctnttggcc antcccctgg gggcntntan cnccccctnt ggtcccntng ggcc          834
```

<210> 36
<211> 814
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(814)
<223> n = A,T,C or G

<400> 36
```
cggncgcttt ccngccgcgc cccgtttcca tgacnaaggc tcccttcang ttaaatacnn    60
cctagnaaac attaatgggt tgctctacta atacatcata cnaaccagta agcctgccca   120
naacgccaac tcaggccatt cctaccaaag gaagaaaggc tggtctctcc accccctgta   180
ggaaaggcct gccttgtaag acaccacaat ncggctgaat ctnaagtctt gtgttttact   240
aatggaaaaa aaaaataaac aanaggtttt gttctcatgg ctgcccaccg cagcctggca   300
ctaaaacanc ccagcgctca cttctgcttg ganaaatatt ctttgctctt ttggacatca   360
ggcttgatgg tatcactgcc acntttccac ccagctgggc ncccttcccc catntttgtc   420
antganctgg aaggcctgaa ncttagtctc caaaagtctc ngcccacaag accggccacc   480
aggggangtc ntttncagtg gatctgccaa anantacccn tatcatcnnt gaataaaaag   540
gcccctgaac ganatgcttc cancancctt taagacccat aatcctngaa ccatggtgcc   600
cttccggtct gatccnaaag gaatgttcct gggtcccant ccctcctttg ttncttacgt   660
tgtnttggac ccntgctngn atnacccaan tganatcccc ngaagcaccc tnccctggc    720
atttganttt cntaaattct ctgccctacn nctgaaagca cnattccctn ggcnccnaan   780
ggngaactca agaaggtctn ngaaaaacca cncn                               814
```

<210> 37
<211> 760
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(760)
<223> n = A,T,C or G

<400> 37
```
gcatgctgct cttcctcaaa gttgttcttg ttgccataac aaccaccata ggtaaagcgg    60
gcgcagtgtt cgctgaaggg gttgtagtac cagcgcggga tgctctcctt gcagagtcct   120
gtgtctggca ggtccacgca atgccctttg tcactgggga aatggatgcg ctggagctcg   180
tcnaanccac tcgtgtattt ttcacangca gcctcctccg aagcntccgg gcagttgggg   240
gtgtcgtcac actccactaa actgtcgatn cancagccca ttgctgcagc ggaactgggt   300
gggctgacag gtgccagaac acactggatn ggcctttcca tggaagggcc tgggggaaat   360
cncctnancc caaactgcct ctcaaaggcc accttgcaca ccccgacagg ctagaaatgc   420
actcttcttc ccaaaggtag ttgttcttgt tgcccaagca ncctccanca aaccaaaanc   480
ttgcaaaatc tgctccgtgg gggtcatnnn taccanggtt ggggaaanaa acccggcngn   540
ganccncctt gtttgaatgc naaggnaata atcctcctgt cttgcttggg tggaanagca   600
caattgaact gttaacnttg ggccgngttc cnctngggtg gtctgaaact aatcaccgtc   660
actggaaaaa ggtangtgcc ttccttgaat tcccaaantt ccctngntt tgggtnnttt   720
ctcctctncc ctaaaaatcg tnttccccc ccntanggcg                          760
```

<210> 38
<211> 724
<212> DNA
<213> Homo sapien

```
        <220>
        <221> misc_feature
        <222> (1)...(724)
        <223> n = A,T,C or G   .

        <400> 38
tttttttttt   tttttttttt   tttttttttt   tttttaaaaa   ccccctccat   tgaatgaaaa        60
cttccnaaat   tgtccaaccc   cctcnnccaa   atnnccattt   ccggggggg g   gttccaaacc       120
caaattaatt   ttgganttta   aattaaatnt   tnattngggg   aanaanccaa   atgtnaagaa       180
aatttaaccc   attatnaact   taaatncctn   gaaacccntg   gnttccaaaa   atttttaacc       240
cttaaatccc   tccgaaattg   ntaanggaaa   accaaattcn   cctaaggctn   tttgaaggtt       300
ngatttaaac   cccccttnant   tnttttnacc   cnngnctnaa   ntatttngnt   tccggtgttt       360
tcctnttaan   cntnggtaac   tcccgntaat   gaannnccct   aanccaatta   aaccgaattt       420
ttttttgaatt   ggaaattccn   ngggaattna   ccggggtttt   tcccntttgg   gggccatncc       480
cccnctttcg   gggtttgggn   ntaggttgaa   tttttnnang   ncccaaaaaa   nccccccaana       540
aaaaaactcc   caagnnttaa   ttngaatntc   cccccttccca   ggccttttgg   gaaaggnggg       600
tttntggggg   ccngggantt   cnttcccccn   ttnccncccc   ccccccnggt   aaanggttat       660
ngnnttttggt   ttttgggccc   cttnanggac   cttccggatn   gaaattaaat   ccccgggncg       720
gccg                                                                            724

        <210> 39
        <211> 751
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(751)
        <223> n = A,T,C or G

        <400> 39
tttttttttt   tttttctttg   ctcacattta   attttttattt   tgattttttt   taatgctgca        60
caacacaata   tttatttcat   ttgtttcttt   tatttcattt   tatttgtttg   ctgctgctgt       120
tttatttatt   tttactgaaa   gtgagaggga   acttttgtgg   ccttttttttcc   tttttctgta       180
ggccgcctta   agctttctaa   atttggaaca   tctaagcaag   ctgaaggaa   aaggggggttt       240
cgcaaaatca   ctcgggggaa   nggaaaggtt   gctttgttaa   tcatgccota   tggtgggtga       300
ttaactgctt   gtacaattac   ntttcacttt   taattaattg   tgctnaangc   tttaattana       360
cttggggggtt   ccctccccan   accaaccccn   ctgacaaaaa   gtgccngccc   tcaaatnatg       420
tcccggcnnt   cnttgaaaca   cacncgcgaa   ngttctcatt   ntccccncnc   caggtnaaaa       480
tgaagggtta   ccatntttaa   cnccacctcc   acntggcnnn   gcctgaatcc   tcnaaaancn       540
ccctcaancn   aattnctnng   ccccggtcnc   gcntnngtcc   cnccccgggct   ccgggaantn       600
cacccccnga   annncnntnnc   naacnaaatt   ccgaaaatat   tcccnntcnc   tcaattcccc       660
cnnagactnt   cctcnncnan   cncaattttc   ttttnntcac   gaacncgnnc   cnnaaaatgn       720
nnnncncctc   cnctngtccn   naatcnccan   c                                         751

        <210> 40
        <211> 753
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(753)
        <223> n = A,T,C or G

        <400> 40
gtggtatttt   ctgtaagatc   aggtgttcct   ccctcgtagg   tttagaggaa   acaccctcat        60
agatgaaaac   cccccccgaga   cagcagcact   gcaactgcca   agcagccggg   gtaggagggg       120
```

```
cgccctatgc acagctgggc ccttgagaca gcagggcttc gatgtcaggc tcgatgtcaa     180
tggtctggaa gcggcggctg tacctgcgta ggggcacacc gtcagggccc accaggaact     240
tctcaaagtt ccaggcaacn tcgttgcgac acaccggaga ccaggtgatn agcttggggt     300
cggtcataan cgcggtggcg tcgtcgctgg gagctggcag ggcctcccgc aggaaggcna     360
ataaaaggtg cgcccccgca ccgttcanct cgcacttctc naanaccatg angttgggct     420
cnaacccacc accannccgg acttccttga nggaattccc aaatctcttc gntcttgggc     480
ttctnctgat gccctanctg gttgcccngn atgccaanca nccccaancc ccggggtcct     540
aaancacccn cctcctcntt tcatctgggt tnttntcccc ggaccntggt tcctctcaag     600
ggancccata tctcnaccan tactcaccnt nccccccccnt gnnacccanc cttctanngn     660
ttcccncccg ncctctggcc cntcaaanan gcttncacna cctgggtctg ccttcccccc     720
tncccctatct gnacccncn tttgtctcan tnt                                 753
```

        <210> 41
        <211> 341
        <212> DNA
        <213> Homo sapien

        <400> 41
```
actatatcca tcacaacaga catgcttcat cccatagact tcttgacata gcttcaaatg      60
agtgaacccca tccttgattt atatacatat atgttctcag tattttggga gcctttccac     120
ttctttaaac cttgttcatt atgaacactg aaaataggaa tttgtgaaga gttaaaaagt     180
tatagcttgt ttacgtagta agttttttgaa gtctacattc aatccagaca cttagttgag     240
tgttaaactg tgattttttaa aaaatatcat ttgagaatat tctttcagag gtattttcat     300
ttttactttt tgattaattg tgttttatat attagggtag t                         341
```

        <210> 42
        <211> 101
        <212> DNA
        <213> Homo sapien

        <400> 42
```
acttactgaa tttagttctg tgctcttcct tatttagtgt tgtatcataa atactttgat      60
gtttcaaaca ttctaaataa ataattttca gtggcttcat a                         101
```

        <210> 43
        <211> 305
        <212> DNA
        <213> Homo sapien

        <400> 43
```
acatctttgt tacagtctaa gatgtgttct taaatcacca ttccttcctg gtcctcaccc      60
tccagggtgg tctcacactg taattagagc tattgaggag tctttacagc aaattaagat     120
tcagatgcct tgctaagtct agagttctag agttatgttt cagaaagtct aagaaaccca     180
cctcttgaga ggtcagtaaa gaggacttaa tatttcatat ctacaaaatg accacaggat     240
tggatacaga acgagagtta tcctggataa ctcagagctg agtacctgcc cgggggccgc     300
tcgaa                                                                 305
```

        <210> 44
        <211> 852
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(852)
        <223> n = A,T,C or G

        <400> 44

```
acataaatat cagagaaaag tagtctttga aatatttacg tccaggagtt ctttgtttct     60
gattatttgg tgtgtgtttt ggtttgtgtc caaagtattg gcagcttcag ttttcatttt    120
ctctccatcc tcggcattc ttcccaaatt tatataccag tcttcgtcca tccacacgct     180
ccagaatttc tcttttgtag taatatctca tagctcggct gagctttca taggtcatgc     240
tgctgttgtt cttcttttta ccccatagct gagccactgc ctctgatttc aagaacctga    300
agacgccctc agatcggtct tcccatttta ttaatcctgg gttcttgtct gggttcaaga    360
ggatgtcgcg gatgaattcc cataagtgag tccctctcgg gttgtgcttt ttggtgtggc    420
acttggcagg ggggtcttgc tcctttttca tatcaggtga ctctgcaaca ggaaggtgac    480
tggtggttgt catggagatc tgagcccggc agaaagtttt gctgtccaac aaatctactg    540
tgctaccata gttggtgtca tataaatagt tctngtcttt ccaggtgttc atgatggaag    600
gctcagtttg ttcagtcttg acaatgacat tgtgtgtgga ctggaacagg tcactactgc    660
actggccgtt ccacttcaga tgctgcaagt tgctgtagag gagntgcccc gccgtccctg    720
ccgcccgggt gaactcctgc aaactcatgc tgcaaaggtg ctcgccgttg atgtcgaact    780
cntggaaagg gatacaattg gcatccagct ggttggtgtc caggaggtga tggagccact    840
cccacacctg gt                                                        852
```

```
<210> 45
<211> 234
<212> DNA
<213> Homo sapien


<400> 45
acaacagacc cttgctcgct aacgacctca tgctcatcaa gttggacgaa tccgtgtccg     60
agtctgacac catccggagc atcagcattg cttcgcagtg ccctaccgcg gggaactctt    120
gcctcgtttc tggctggggt ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg    180
tgaacgtgtc ggtggtgtct gaggaggtct gcagtaagct ctatgacccg ctgt          234
```

```
<210> 46
<211> 590
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(590)
<223> n = A,T,C or G

<400> 46
acttttattt taaatgtttta taaggcagat ctatgagaat gatagaaaac atggtgtgta     60
atttgatagc aatatttttgg agattacaga gttttagtaa ttaccaatta cacagttaaa    120
aagaagataa tatattccaa gcanatacaa aatatctaat gaaagatcaa ggcaggaaaa    180
tgantataac taattgacaa tggaaaatca attttaatgt gaattgcaca ttatcctttta    240
aaagctttca aaanaaanaa ttattgcagt ctanttaatt caaacagtgt taaatggtat    300
caggataaan aactgaaggg canaaagaat taattttcac ttcatgtaac ncacccanat    360
ttacaatggc ttaaatgcan ggaaaaagca gtggaagtag ggaagtantc aaggtctttc    420
tggtctctaa tctgccttac tctttgggtg tggctttgat cctctggaga cagctgccag    480
ggctcctgtt atatccacaa tcccagcagc aagatgaagg gatgaaaaag gacacatgct    540
gccttccttt gaggagactt catctcactg gccaacactc agtcacatgt                590
```

```
<210> 47
<211> 774
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(774)
<223> n = A,T,C or G
```

```
       <400> 47
acaaggggggc ataatgaagg agtgggggana gattttaaag aaggaaaaaa aacgaggccc        60
tgaacagaat tttcctgnac aacggggctt caaaataatt ttcttgggga ggttcaagac        120
gcttcactgc ttgaaactta aatggatgtg ggacanaatt ttctgtaatg accctgaggg        180
cattacagac gggactctgg gaggaaggat aaacagaaag gggacaaagg ctaatcccaa        240
aacatcaaag aaaggaaggt ggcgtcatac ctcccagcct acacagttct ccagggctct        300
cctcatccct ggaggacgac agtggaggaa caactgacca tgtccccagg ctcctgtgtg        360
ctggctcctg gtcttcagcc cccagctctg gaagcccacc ctctgctgat cctgcgtggc        420
ccacactcct tgaacacaca tccccaggtt atattcctgg acatggctga acctcctatt        480
cctacttccg agatgccttg ctccctgcag cctgtcaaaa tcccactcac cctccaaacc        540
acggcatggg aagcctttct gacttgcctg attactccag catcttggaa caatccctga        600
ttccccactc cttagaggca agatagggtg gttaagagta gggctggacc acttggagcc        660
aggctgctgg cttcaaattn tggctcattt acgagctatg ggaccttggg caagtnatct        720
tcacttctat gggcntcatt ttgttctacc tgcaaaatgg gggataataa tagt            774
```

       <210> 48
       <211> 124
       <212> DNA
       <213> Homo sapien

       <220>
       <221> misc_feature
       <222> (1)...(124)
       <223> n = A,T,C or G

```
       <400> 48
canaaattga aattttataa aaaggcattt ttctcttata tccataaaat gatataattt        60
ttgcaantat anaaatgtgt cataaattat aatgttcctt aattacagct caacgcaact        120
tggt                                                                    124
```

       <210> 49
       <211> 147
       <212> DNA
       <213> Homo sapien

       <220>
       <221> misc_feature
       <222> (1)...(147)
       <223> n = A,T,C or G

```
       <400> 49
gccgatgcta ctattttatt gcaggaggtg ggggtgtttt tattattctc tcaacagctt        60
tgtggctaca ggtggtgtct gactgcatna aaaanttttt tacgggtgat tgcaaaaatt        120
ttagggcacc catatcccaa gcantgt                                            147
```

       <210> 50
       <211> 107
       <212> DNA
       <213> Homo sapien

```
       <400> 50
acattaaatt aataaaagga ctgttggggt tctgctaaaa cacatggctt gatatattgc        60
atggtttgag gttaggagga gttaggcata tgttttggga gaggggt                     107
```

       <210> 51
       <211> 204
       <212> DNA

<213> Homo sapien

<400> 51
gtcctaggaa gtctagggga cacacgactc tggggtcacg gggccgacac acttgcacgg   60
cgggaaggaa aggcagagaa gtgacaccgt caggggggaaa tgacagaaag gaaaatcaag   120
gccttgcaag gtcagaaagg ggactcaggg cttccaccac agccctgccc cacttggcca   180
cctccctttt gggaccagca atgt   204

        <210> 52
        <211> 491
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(491)
        <223> n = A,T,C or G

        <400> 52
acaaagataa catttatctt ataacaaaaa tttgatagtt ttaaaggtta gtattgtgta   60
gggtatttttc caaaagacta aagagataac tcaggtaaaa agttagaaat gtataaaaca   120
ccatcagaca ggttttttaaa aaacaacata ttacaaaatt agacaatcat ccttaaaaaa   180
aaaacttctt gtatcaattt cttttgttca aaatgactga cttaantatt tttaaatatt   240
tcanaaacac ttcctcaaaa attttcaana tggtagcttt canatgtncc ctcagtccca   300
atgttgctca gataaataaa tctcgtgaga acttaccacc caccacaagc tttctggggc   360
atgcaacagt gtcttttctt tnctttttct tttttttttt ttacaggcac agaaactcat   420
caattttatt tggataacaa agggtctcca aattatattg aaaaataaat ccaagttaat   480
atcactcttg t   491

        <210> 53
        <211> 484
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(484)
        <223> n = A,T,C or G

        <400> 53
acataattta gcagggctaa ttaccataag atgctattta ttaanaggtn tatgatctga   60
gtattaacag ttgctgaagt ttggtatttt tatgcagcat tttcttttg ctttgataac   120
actacagaac ccttaaggac actgaaaatt agtaagtaaa gttcagaaac attagctgct   180
caatcaaatc tctacataac actatagtaa ttaaaacgtt aaaaaaaagt gttgaaatct   240
gcactagtat anaccgctcc tgtcaggata anactgcttt ggaacagaaa gggaaaaanc   300
agctttgant ttctttgtgc tgatangagg aaaggctgaa ttaccttgtt gcctctccct   360
aatgattggc aggtcnggta aatnccaaaa catattccaa ctcaacactt cttttccncg   420
tancttgant ctgtgtattc caggancagg cggatggaat gggccagccc ncggatgttc   480
cant   484

        <210> 54
        <211> 151
        <212> DNA
        <213> Homo sapien

        <400> 54
actaaacctc gtgcttgtga actccataca gaaaacggtg ccatccctga acacggctgg   60
ccactgggta tactgctgac aaccgcaaca acaaaaacac aaatccttgg cactggctag   120

```
tctatgtcct ctcaagtgcc tttttgtttg t                                151

        <210> 55
        <211> 91
        <212> DNA
        <213> Homo sapien

        <400> 55
acctggcttg tctccgggtg gttcccggcg cccccacgg tccccagaac ggacactttc    60
gccctccagt ggatactcga gccaaagtgg t                                 91

        <210> 56
        <211> 133
        <212> DNA
        <213> Homo sapien

        <400> 56
ggcggatgtg cgttggttat atacaaatat gtcattttat gtaagggact tgagtatact   60
tggatttttg gtatctgtgg gttgggggga cggtccagga accaataccc catggatacc  120
aagggacaac tgt                                                      133

        <210> 57
        <211> 147
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(147)
        <223> n = A,T,C or G

        <400> 57
actctggaga acctgagccg ctgctccgcc tctgggatga ggtgatgcan gcngtggcgc   60
gactgggagc tgagcccttc cctttgcgcc tgcctcagag gattgttgcc gacntgcana  120
tctcantggg ctggatncat gcagggt                                      147

        <210> 58
        <211> 198
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(198)
        <223> n = A,T,C or G

        <400> 58
acagggatat aggtttnaag ttattgtnat tgtaaaatac attgaatttt ctgtatactc   60
tgattacata catttatcct ttaaaaaaga tgtaaatctt aatttttatg ccatctatta  120
atttaccaat gagttacctt gtaaatgaga agtcatgata gcactgaatt ttaactagtt  180
ttgacttcta agtttggt                                                198

        <210> 59
        <211> 330
        <212> DNA
        <213> Homo sapien

        <400> 59
```

```
acaacaaatg ggttgtgagg aagtcttatc agcaaaactg gtgatggcta ctgaaaagat      60
ccattgaaaa ttatcattaa tgattttaaa tgacaagtta tcaaaaactc actcaatttt     120
cacctgtgct agcttgctaa aatgggagtt aactctagag caaatatagt atcttctgaa     180
tacagtcaat aaatgacaaa gccagggcct acaggtggtt tccagacttt ccagacccag     240
cagaaggaat ctattttatc acatggatct ccgtctgtgc tcaaaatacc taatgatatt     300
tttcgtcttt attggacttc tttgaagagt                                      330
```

        <210> 60
        <211> 175
        <212> DNA
        <213> Homo sapien

        <400> 60
```
accgtgggtg ccttctacat tcctgacggc tccttcacca acatctggtt ctacttcggc      60
gtcgtgggct ccttcctctt catcctcatc cagctggtgc tgctcatcga ctttgcgcac     120
tcctggaacc agcggtggct gggcaaggcc gaggagtgcg attcccgtgc ctggt          175
```

        <210> 61
        <211> 154
        <212> DNA
        <213> Homo sapien

        <400> 61
```
accccacttt tcctcctgtg agcagtctgg acttctcact gctacatgat gagggtgagt      60
ggttgttgct cttcaacagt atcctcccct ttccggatct gctgagccgg acagcagtgc     120
tggactgcac agccccgggg ctccacattg ctgt                                 154
```

        <210> 62
        <211> 30
        <212> DNA
        <213> Homo sapien

        <400> 62
```
cgctcgagcc ctatagtgag tcgtattaga                                       30
```

        <210> 63
        <211> 89
        <212> DNA
        <213> Homo sapien

        <400> 63
```
acaagtcatt tcagcaccct ttgctcttca aaactgacca tcttttatat ttaatgcttc      60
ctgtatgaat aaaaatggtt atgtcaagt                                        89
```

        <210> 64
        <211> 97
        <212> DNA
        <213> Homo sapien

        <400> 64
```
accggagtaa ctgagtcggg acgctgaatc tgaatccacc aataaataaa ggttctgcag      60
aatcagtgca tccaggattg gtccttggat ctggggt                              97
```

        <210> 65
        <211> 377
        <212> DNA
        <213> Homo sapien

```
        <220>
        <221> misc_feature
        <222> (1)...(377)
        <223> n = A,T,C or G

        <400> 65
acaacaanaa ntcccttctt taggccactg atggaaacct ggaacccccct tttgatggca        60
gcatggcgtc ctaggccttg acacagcggc tggggtttgg gctntcccaa accgcacacc       120
ccaaccctgg tctacccaca nttctggcta tgggctgtct ctgccactga acatcagggt       180
tcggtcataa natgaaatcc caanggggac agaggtcagt agaggaagct caatgagaaa       240
ggtgctgttt gctcagccag aaaacagctg cctggcattc gccgctgaac tatgaacccg       300
tgggggtgaa ctaccccccan gaggaatcat gcctgggcga tgcaanggtg ccaacaggag       360
gggcgggagg agcatgt                                                       377

        <210> 66
        <211> 305
        <212> DNA
        <213> Homo sapien

        <400> 66
acgcctttcc ctcagaattc agggaagaga ctgtcgcctg ccttcctccg ttgttgcgtg        60
agaacccgtg tgcccccttcc caccatatcc accctcgctc catctttgaa ctcaaacacg       120
aggaactaac tgcaccctgg tcctctcccc agtccccagt tcaccctcca tccctcacct       180
tcctccactc taagggatat caacactgcc cagcacaggg gccctgaatt tatgtggttt       240
ttatatattt tttaataaga tgcactttat gtcatttttt aataaagtct gaagaattac       300
tgttt                                                                    305

        <210> 67
        <211> 385
        <212> DNA
        <213> Homo sapien

        <400> 67
actacacaca ctccacttgc ccttgtgaga cactttgtcc cagcacttta ggaatgctga        60
ggtcggacca gccacatctc atgtgcaaga ttgcccagca gacatcaggt ctgagagttc       120
cccttttaaa aaagggggact tgcttaaaaa agaagtctag ccacgattgt gtagagcagc       180
tgtgctgtgc tggagattca cttttgagag agttctcctc tgagacctga tctttagagg       240
ctgggcagtc ttgcacatga gatggggctg gtctgatctc agcactcctt agtctgcttg       300
cctctcccag ggccccagcc tggccacacc tgcttacagg gcactctcag atgcccatac       360
catagtttct gtgctagtgg accgt                                              385

        <210> 68
        <211> 73
        <212> DNA
        <213> Homo sapien

        <400> 68
acttaaccag atatattttt accccagatg gggatattct ttgtaaaaaa tgaaaataaa        60
gtttttttaa tgg                                                           73

        <210> 69
        <211> 536
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(536)
```

```
    <223> n = A,T,C or G

    <400> 69
actagtccag tgtggtggaa ttccattgtg ttgggggctc tcaccctcct ctcctgcagc        60
tccagctttg tgctctgcct ctgaggagac catggcccag catctgagta ccctgctgct       120
cctgctggcc accctagctg tggccctggc ctggagcccc aaggaggagg ataggataat       180
cccgggtggc atctataacg cagacctcaa tgatgagtgg gtacagcgtg cccttcactt       240
cgccatcagc gagtataaca aggccaccaa agatgactac tacagacgtc cgctgcgggt       300
actaagagcc aggcaacaga ccgttggggg ggtgaattac ttcttcgacg tagaggtggg       360
ccgaaccata tgtaccaagt cccagcccaa cttggacacc tgtgccttcc atgaacagcc       420
agaactgcag aagaaacagt tgtgctcttt cgagatctac gaagttccct ggggagaaca       480
gaangtccct gggtgaaatc caggtgtcaa gaaatcctan ggatctgttg ccaggc           536

    <210> 70
    <211> 477
    <212> DNA
    <213> Homo sapien

    <400> 70
atgacccctta acaggggccc tctcagccct cctaatgacc tccggcctag ccatgtgatt        60
tcacttccac tccataacgc tcctcatact aggcctacta accaacacac taaccatata       120
ccaatgatgg cgcgatgtaa cacgagaaag cacataccaa ggccaccaca caccacctgt       180
ccaaaaaggc cttcgatacg ggataatcct atttattacc tcagaagttt ttttcttcgc       240
agggattttt ctgagccttt taccactcca gcctagcccc taccccccaa ctaggagggc       300
actggcccce aacaggcatc accccgctaa atcccctaga agtcccactc ctaaacacat       360
ccgtattact cgcatcagga gtatcaatca cctgagctca ccatagtcta atagaaaaca       420
accgaaacca aattattcaa agcactgctt attacaattt tactgggtct ctattttt         477

    <210> 71
    <211> 533
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(533)
    <223> n = A,T,C or G

    <400> 71
agagctatag gtacagtgtg atctcagctt tgcaaacaca ttttctacat agatagtact        60
aggtattaat agatatgtaa agaaagaaat cacaccatta ataatggtaa gattggttta       120
tgtgatttta gtggtatttt tggcacccctt atatatgttt tccaaacttt cagcagtgat ,     180
attatttcca taacttaaaa agtgagtttg aaaaagaaaa tctccagcaa gcatctcatt       240
taaataaagg tttgtcatct ttaaaaatac agcaatatgt gacttttaa aaaagctgtc       300
aaataggtgt gaccctacta ataattatta gaaatacatt taaaaacatc gagtacctca       360
agtcagtttg ccttgaaaaa tatcaaatat aactcttaga gaaatgtaca taaaagaatg       420
cttcgtaatt ttggagtang aggttccctc ctcaattttg tatttttaaa aagtacatgg       480
taaaaaaaaa aattcacaac agtatataag gctgtaaaat gaagaattct gcc             533

    <210> 72
    <211> 511
    <212> DNA
    <213> Homo sapien

    <220>
    <221> misc_feature
    <222> (1)...(511)
    <223> n = A,T,C or G
```

```
      <400> 72
tattacggaa aaacacacca cataattcaa ctancaaaga anactgcttc agggcgtgta      60
aaatgaaagg cttccaggca gttatctgat taaagaacac taaaagaggg acaaggctaa     120
aagccgcagg atgtctacac tatancaggc gctatttggg ttggctggag gagctgtgga     180
aaacatggan agattggtgc tgganatcgc cgtggctatt cctcattgtt attacanagt     240
gaggttctct gtgtgcccac tggtttgaaa accgttctnc aataatgata gaatagtaca     300
cacatgagaa ctgaaatggc ccaaacccag aaagaaagcc caactagatc ctcagaanac     360
gcttctaggg acaataaccg atgaagaaaa gatggcctcc ttgtgccccc gtctgttatg     420
atttctctcc attgcagcna naaacccgtt cttctaagca aacncaggtg atgatggcna     480
aaatacaccc cctcttgaag naccnggagg a                                    511
```

```
      <210> 73
      <211> 499
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(499)
      <223> n = A,T,C or G
```

```
      <400> 73
cagtgccagc actggtgcca gtaccagtac caataacagt gccagtgcca gtgccagcac      60
cagtggtggc ttcagtgctg gtgccagcct gaccgccact ctcacatttg ggctcttcgc     120
tggccttggt ggagctggtg ccagcaccag tggcagctct ggtgcctgtg gtttctccta     180
caagtgagat tttagatatt gttaatcctg ccagtctttc tcttcaagcc agggtgcatc     240
ctcagaaacc tactcaacac agcactctag gcagccacta tcaatcaatt gaagttgaca     300
ctctgcatta aatctatttg ccatttctga aaaaaaaaaa aaaaaaaggg cggccgctcg     360
antctagagg gcccgtttaa acccgctgat cagcctcgac tgtgccttct anttgccagc     420
catctgttgt ttgcccctcc cccgntgcct tccttgaccc tggaaagtgc cactcccact     480
gtccttttcct aantaaaat                                                 499
```

```
      <210> 74
      <211> 537
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(537)
      <223> n = A,T,C or G
```

```
      <400> 74
tttcatagga gaacacactg aggagatact tgaagaattt ggattcagcc gcgaagagat      60
ttatcagctt aactcagata aaatcattga aagtaataag gtaaaagcta gtctctaact     120
tccaggccca cggctcaagt gaatttgaat actgcattta cagtgtagag taacacataa     180
cattgtatgc atggaaacat ggaggaacag tattacagtg tcctaccact ctaatcaaga     240
aaagaattac agactctgat tctacagtga tgattgaatt ctaaaaatgg taatcattag     300
ggcttttgat ttataanact ttgggtactt atactaaatt atggtagtta tactgccttc     360
cagtttgctt gatatatttg ttgatattaa gattcttgac ttatattttg aatgggttct     420
actgaaaaan gaatgatata ttcttgaaga catcgatata catttattta cactcttgat     480
tctacaatgt agaaaatgaa ggaaatgccc caaattgtat ggtgataaaa gtcccgt        537
```

```
      <210> 75
      <211> 467
      <212> DNA
      <213> Homo sapien
```

```
        <220>
        <221> misc_feature
        <222> (1)...(467)
        <223> n = A,T,C or G

        <400> 75
caaanacaat tgttcaaaag atgcaaatga tacactactg ctgcagctca caaacacctc      60
tgcatattac acgtacctcc tcctgctcct caagtagtgt ggtctatttt gccatcatca     120
cctgctgtct gcttagaaga acggctttct gctgcaangg agagaaatca taacagacgg     180
tggcacaagg aggccatctt ttcctcatcg gttattgtcc ctagaagcgt cttctgagga     240
tctagttggg ctttctttct gggtttgggc catttcantt ctcatgtgtg tactattcta     300
tcattattgt ataacggttt tcaaaccngt gggcacncag agaacctcac tctgtaataa     360
caatgaggaa tagccacggt gatctccagc accaaatctc tccatgttnt tccagagctc     420
ctccagccaa cccaaatagc cgctgctatn gtgtagaaca tccctgn                   467


        <210> 76
        <211> 400
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(400)
        <223> n = A,T,C or G

        <400> 76
aagctgacag cattcgggcc gagatgtctc gctccgtggc cttagctgtg ctcgcgctac      60
tctctctttc tggcctggag gctatccagc gtactccaaa gattcaggtt tactcacgtc     120
atccagcaga gaatggaaag tcaaatttcc tgaattgcta tgtgtctggg tttcatccat     180
ccgacattga agttgactta ctgaagaatg gagagagaat tgaaaaagtg gagcattcag     240
acttgtcttt cagcaaggac tggtctttct atctcttgta ctacactgaa ttcacccca     300
ctgaaaaaga tgagtatgcc tgccgtgtga accatgtgac tttgtcacag cccaagatng     360
ttnagtggga tcganacatg taagcagcan catgggaggt                           400


        <210> 77
        <211> 248
        <212> DNA
        <213> Homo sapien

        <400> 77
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc cggcggggga tgcgaggctc ggagcaccct tgcccggctg tgattgctgc     120
caggcactgt tcatctcagc ttttctgtcc ctttgctccc ggcaagcgct tctgctgaaa     180
gttcatatct ggagcctgat gtcttaacga ataaaggtcc catgctccac ccgaaaaaaa     240
aaaaaaaa                                                              248


        <210> 78
        <211> 201
        <212> DNA
        <213> Homo sapien

        <400> 78
actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct acctttaaca      60
tcacccagac cccgccctgc ccgtgcccca cgctgctgct aacgacagta tgatgcttac     120
tctgctactc ggaaactatt tttatgtaat taatgtatgc tttcttgttt ataaatgcct     180
gatttaaaaa aaaaaaaaaa a                                               201
```

```
<210> 79
<211> 552
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(552)
<223> n = A,T,C or G

<400> 79
tccttttgtt aggttttga gacaaccta gacctaaact gtgtcacaga cttctgaatg    60
tttaggcagt gctagtaatt tcctcgtaat gattctgtta ttactttcct attctttatt   120
cctctttctt ctgaagatta atgaagttga aaattgaggt ggataaatac aaaaaggtag   180
tgtgatagta taagtatcta agtgcagatg aaagtgtgtt atatatatcc attcaaaatt   240
atgcaagtta gtaattactc agggttaact aaattacttt aatatgctgt tgaacctact   300
ctgttccttg gctagaaaaa attataaaca ggactttgtt agtttgggaa gccaaattga   360
taatattcta tgttctaaaa gttgggctat acataaanta tnaagaaata tggaatttta   420
ttcccaggaa tatggggttc atttatgaat antacccggg anagaagttt tgantnaaac   480
cngttttggt taatacgtta atatgtcctn aatnaacaag gcntgactta tttccaaaaa   540
aaaaaaaaaa aa                                                        552


<210> 80
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

<400> 80
acagggattt gagatgctaa ggccccagag atcgtttgat ccaaccctct tattttcaga    60
ggggaaaatg gggcctagaa gttacagagc atctagctgg tgcgctggca cccctggcct   120
cacacagact cccgagtagc tgggactaca ggcacacagt cactgaagca ggccctgttt   180
gcaattcacg ttgccacctc caacttaaac attcttcata tgtgatgtcc ttagtcacta   240
aggttaaact ttcccaccca gaaaaggcaa cttagataaa atcttagagt actttcatac   300
tcttctaagt cctcttccag cctcactttg agtcctcctt gggggttgat aggaantntc   360
tcttggcttt ctcaataaaa tctctatcca tctcatgttt aatttggtac gcntaaaaat   420
gctgaaaaaa ttaaaatgtt ctggtttcnc tttaaaaaaa aaaaaaaaa aaaaaa         476


<210> 81
<211> 232
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(232)
<223> n = A,T,C or G

<400> 81
ttttttttg tatgccntcn ctgtggngtt attgttgctg ccaccctgga ggagcccagt    60
ttcttctgta tctttctttt ctggggatc ttcctggctc tgcccctcca ttcccagcct   120
ctcatcccca tcttgcactt ttgctagggt tggaggcgct ttcctggtag ccctcagag    180
actcagtcag cgggaataag tcctaggggt ggggggtgtg gcaagccggc ct           232
```

```
      <210> 82
      <211> 383
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(383)
      <223> n = A,T,C or G

      <400> 82
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc          60
agtaccagta ccaataacat gccagtgcca gtgccagcac cagtggtggc ttcagtgctg         120
gtgccagcct gaccgccact ctcacatttg ggctcttcgc tggccttggt ggagctggtg         180
ccagcaccag tggcagctct ggtgcctgtg gtttctccta caagtgagat tttagatatt         240
gttaatcctg ccagtctttc tcttcaagcc agggtgcatc ctcagaaacc tactcaacac         300
agcactctng gcagccacta tcaatcaatt gaagttgaca ctctgcatta aatctatttg         360
ccatttcaaa aaaaaaaaa aaa                                                   383


      <210> 83
      <211> 494
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(494)
      <223> n = A,T,C or G

      <400> 83
accgaattgg gaccgctggc ttataagcga tcatgtcctc cagtattacc tcaacgagca          60
gggagatcga gtctatacgc tgaagaaatt tgacccgatg ggacaacaga cctgctcagc         120
ccatcctgct cggttctccc cagatgacaa atactctcga caccgaatca ccatcaagaa         180
acgcttcaag gtgctcatga cccagcaacc gcgccctgtc ctctgagggt ccttaaactg         240
atgtcttttc tgccacctgt taccccctcgg agactccgta accaaactct tcggactgtg        300
agccctgatg ccttttttgcc agccatactc tttggcntcc agtctctcgt ggcgattgat         360
tatgcttgtg tgaggcaatc atggtggcat cacccatnaa gggaacacat ttganttttt         420
tttcncatat tttaaattac naccagaata nttcagaata aatgaattga aaaactctta         480
aaaaaaaaaa aaaa                                                           494


      <210> 84
      <211> 380
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(380)
      <223> n = A,T,C or G

      <400> 84
gctggtagcc tatggcgtgg ccacggangg gctcctgagg cacgggacag tgacttccca          60
agtatcctgc gccgcgtctt ctaccgtccc tacctgcaga tcttcgggca gattccccag         120
gaggacatgg acgtggccct catggagcac agcaactgct cgtcggagcc cggcttctgg         180
gcacaccctc ctggggccca ggcgggcacc tgcgtctccc agtatgccaa ctggctggtg         240
gtgctgctcc tcgtcatctt cctgctcgtg gccaacatcc tgctggtcac ttgctcattg         300
ccatgttcag ttacacattc ggcaaagtac agggcaacag cnatctctac tgggaaggcc         360
agcgttnccg cctcatccgg                                                     380
```

```
<210> 85
<211> 481
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(481)
<223> n = A,T,C or G

<400> 85
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc       60
tnccatcgtc atactgtagg tttgccacca cctcctgcat cttggggcgg ctaatatcca      120
ggaaactctc aatcaagtca ccgtcnatna aacctgtggc tggttctgtc ttccgctcgg      180
tgtgaaagga tctccagaag gagtgctcga tcttccccac acttttgatg actttattga      240
gtcgattctg catgtccagc aggaggttgt accagctctc tgacagtgag gtcaccagcc      300
ctatcatgcc nttgaacgtg ccgaagaaca ccgagccttg tgtggggggt gnagtctcac      360
ccagattctg cattaccaga nagccgtggc aaaaganatt gacaactcgc ccaggnngaa      420
aaagaacacc tcctggaagt gctngccgct cctcgtccnt tggtggnngc gcntnccttt      480.
t                                                                       481

<210> 86
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 86
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgctg agaattcatt       60
acttggaaaa gcaacttnaa gcctggacac tggtattaaa attcacaata tgcaacactt      120
taaacagtgt gtcaatctgc tcccttactt tgtcatcacc agtctgggaa taagggtatg      180
ccctattcac acctgttaaa agggcgctaa gcatttttga ttcaacatct ttttttttga      240
cacaagtccg aaaaaagcaa aagtaaacag ttnttaattt gttagccaat tcactttctt      300
catgggacag agccatttga tttaaaaagc aaattgcata atattgagct ttgggagctg      360
atatntgagc ggaagantag cctttctact tcaccagaca caactccttt catattggga      420
tgttnacnaa agttatgtct cttacagatg ggatgctttt gtggcaattc tg              472

<210> 87
<211> 413
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(413)
<223> n = A,T,C or G

<400> 87
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg       60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg      120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct      180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt      240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc cttgactagg      300
```

```
ggggacaaag aaaagcanaa ctgaacatna gaaacaattn cctggtgaga aattncataa        360
acagaaattg ggtngtatat tgaaananng catcattnaa acgttttttt ttt             413
```

```
        <210> 88
        <211> 448
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(448)
        <223> n = A,T,C or G

        <400> 88
cgcagcgggt cctctctatc tagctccagc ctctcgcctg ccccactccc cgcgtcccgc         60
gtcctagccn accatggccg ggcccctgcg cgccccgctg ctcctgctgg ccatcctggc        120
cgtggccctg gccgtgagcc ccgcggccgg ctccagtccc ggcaagccgc cgcgcctggt        180
gggaggccca tggacccccgc gtggaagaag aaggtgtgcg gcgtgcactg gactttgccg        240
tcggcnanta caacaaaccc gcaacnactt ttaccnagcn cgcgctgcag gttgtgccgc        300
cccaancaaa ttgttactng gggtaantaa ttcttggaag ttgaacctgg gccaaacnng        360
tttaccagaa ccnagccaat tngaacaatt nccctccat aacagcccct tttaaaaagg        420
gaancantcc tgntctttc caaatttt                                             448
```

```
        <210> 89
        <211> 463
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(463)
        <223> n = A,T,C or G

        <400> 89
gaattttgtg cactggccac tgtgatggaa ccattgggcc aggatgcttt gagtttatca         60
gtagtgattc tgccaaagtt ggtgttgtaa catgagtatg taaaatgtca aaaaattagc        120
agaggtctag gtctgcatat cagcagacag tttgtccgtg tattttgtag ccttgaagtt        180
ctcagtgaca agttnnttct gatgcgaagt tctnattcca gtgttttagt cctttgcatc        240
tttnatgttn agacttgcct ctntnaaatt gcttttgtnt tctgcaggta ctatctgtgg        300
tttaacaaaa tagaannact tctctgcttn gaanatttga atatcttaca tctnaaaatn        360
aattctctcc ccatannaaa acccangccc ttgggganaat ttgaaaaang gntccttcnn        420
aattcnnana anttcagntn tcatacaaca naacngganc ccc                          463
```

```
        <210> 90
        <211> 400
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(400)
        <223> n = A,T,C or G

        <400> 90
agggattgaa ggtctnttnt actgtcggac tgttcancca ccaactctac aagttgctgt         60
cttccactca ctgtctgtaa gcntnttaac ccagactgta tcttcataaa tagaacaaat        120
tcttcaccag tcacatcttc taggaccttt ttggattcag ttagtataag ctcttccact        180
tcctttgtta agacttcatc tggtaaagtc ttaagttttg tagaaaggaa tttaattgct        240
```

33

```
cgttctctaa caatgtcctc tccttgaagt atttggctga acaacccacc tnaagtccct      300
ttgtgcatcc attttaaata tacttaatag ggcattggtn cactaggtta aattctgcaa      360
gagtcatctg tctgcaaaag ttgcgttagt atatctgcca                            400
```

```
        <210> 91
        <211> 480
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(480)
        <223> n = A,T,C or G

        <400> 91
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact      60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac      120
atgcctcttt gactaccgtg tgccagtgct ggtgattctc acacacctcc nnccgctctt      180
tgtggaaaaa ctggcacttg nctggaacta gcaagacatc acttacaaat tcacccacga      240
gacacttgaa aggtgtaaca aagcgactct tgcattgctt tttgtccctc cggcaccagt      300
tgtcaatact aacccgctgg tttgcctcca tcacatttgt gatctgtagc tctggataca      360
tctcctgaca gtactgaaga acttcttctt ttgtttcaaa agcaactctt ggtgcctgtt      420
ngatcaggtt cccatttccc agtccgaatg ttcacatggc atatnttact tcccacaaaa      480
```

```
        <210> 92
        <211> 477 .
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(477)
        <223> n = A,T,C or G

        <400> 92
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact      60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcctt      120
cccacgcagg cagcagcggg gccggtcaat gaactccact cgtggcttgg ggttgacggt      180
taantgcagg aagaggctga ccacctcgcg gtccaccagg atgcccgact gtgcgggacc      240
tgcagcgaaa ctcctcgatg gtcatgagcg ggaagcgaat gangcccagg gccttgccca      300
gaaccttccg cctgttctct ggcgtcacct gcagctgctg ccgctnacac tcggcctcgg      360
accagcggac aaacggcgtt gaacagccgc acctcacgga tgcccantgt gtcgcgctcc      420
aggaacggcn ccagcgtgtc caggtcaatg tcggtgaanc ctccgcgggt aatggcg        477
```

```
        <210> 93
        <211> 377
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(377)
        <223> n = A,T,C or G

        <400> 93
gaacggctgg accttgcctc gcattgtgct gctggcagga ataccttggc aagcagctcc      60
agtccgagca gccccagacc gctgccgccc gaagctaagc ctgcctctgg ccttcccctc      120
cgcctcaatg cagaaccant agtgggagca ctgtgtttag agttaagagt gaacactgtn      180
```

```
tgattttact tgggaatttc ctctgttata tagctttccc caatgctaat ttccaaacaa      240
caacaacaaa ataacatgtt tgcctgttna gttgtataaa agtangtgat tctgtatnta      300
aagaaaatat tactgttaca tatactgctt gcaanttctg tatttattgg tnctctggaa      360
ataaatatat tattaaa                                                     377
```

<210> 94
<211> 495
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(495)
<223> n = A,T,C or G

<400> 94
```
cccttttgagg ggttagggtc cagttcccag tggaagaaac aggccaggag aantgcgtgc      60
cgagctgang cagatttccc acagtgaccc cagagccctg ggctatagtc tctgacccct     120
ccaaggaaag accaccttct ggggacatgg gctggagggc aggacctaga ggcaccaagg     180
gaaggcccca ttccggggct gttccccgag gaggaaggga aggggctctg tgtgcccccc     240
acgaggaana ggccctgant cctgggatca nacacccctt cacgtgtatc cccacacaaa     300
tgcaagctca ccaaggtccc ctctcagtcc cttccctaca ccctgaacgg ncactggccc     360
acacccaccc agancancca cccgccatgg ggaatgtnct caaggaatcg cngggcaacg     420
tggactctng tcccnnaagg gggcagaatc tccaatagan gganngaacc cttgctnana     480
aaaaaaaana aaaaa                                                       495
```

<210> 95
<211> 472
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(472)
<223> n = A,T,C or G

<400> 95
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ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt     120
tagctgtttt gagttgattc gcaccactgc accacaactc aatatgaaaa ctatttnact     180
tatttattat cttgtgaaaa gtatacaatg aaaattttgt tcatactgta tttatcaagt     240
atgatgaaaa gcaatagata tatattcttt tattatgttn aattatgatt gccattatta     300
atcggcaaaa tgtggagtgt atgttctttt cacagtaata tatgcctttt gtaacttcac     360
ttggttattt tattgtaaat gaattacaaa attcttaatt taagaaaatg gtangttata     420
tttanttcan taatttcttt ccttgtttac gttaattttg aaaagaatgc at            472
```

<210> 96
<211> 476
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(476)
<223> n = A,T,C or G

<400> 96
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ctgaagcatt tcttcaaact tntctacttt tgtcattgat acctgtagta agttgacaat      60
```

```
gtggtgaaat ttcaaaatta tatgtaactt ctactagttt tactttctcc cccaagtctt      120
ttttaactca tgatttttac acacacaatc cagaacttat tatatagcct ctaagtcttt      180
attcttcaca gtagatgatg aaagagtcct ccagtgtctt gngcanaatg ttctagntat      240
agctggatac atacngtggg agttctataa actcatacct cagtgggact naaccaaaat      300
tgtgttagtc tcaattccta ccacactgag ggagcctccc aaatcactat attcttatct      360
gcaggtactc ctccagaaaa acngacaggg caggcttgca tgaaaaagtn acatctgcgt      420
tacaaagtct atcttcctca nangtctgtn aaggaacaat ttaatcttct agcttt         476
```

        <210> 97
        <211> 479
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(479)
        <223> n = A,T,C or G

        <400> 97
```
actctttcta atgctgatat gatcttgagt ataagaatgc atatgtcact agaatggata      60
aaataatgct gcaaacttaa tgttcttatg caaaatggaa cgctaatgaa acacagctta      120
caatcgcaaa tcaaaactca caagtgctca tctgttgtag atttagtgta ataagactta      180
gattgtgctc cttcggatat gattgtttct canatcttgg gcaatnttcc ttagtcaaat      240
caggctacta gaattctgtt attggatatn tgagagcatg aaatttttaa naatacactt      300
gtgattatna aattaatcac aaatttcact tatacctgct atcagcagct agaaaaacat      360
ntnnttttta natcaaagta ttttgtgttt ggaantgtnn aaatgaaatc tgaatgtggg      420
ttcnatctta tttttcccn gacnactant tncttttta gggnctattc tganccatc       479
```

        <210> 98
        <211> 461
        <212> DNA
        <213> Homo sapien

        <400> 98
```
agtgacttgt cctccaacaa aacccttga tcaagtttgt ggcactgaca atcagaccta       60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca      120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga      180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagctta       240
tgaagccact ctgaacacgc tggttatcta gatgagaaca gagaaataaa gtcagaaaat      300
ttacctggag aaaagaggct ttggctgggg accatcccat tgaaccttct cttaaggact      360
ttaagaaaaa ctaccacatg ttgtgtatcc tggtgccggc cgtttatgaa ctgaccaccc      420
tttggaataa tcttgacgct cctgaacttg ctcctctgcg a                         461
```

        <210> 99
        <211> 171
        <212> DNA
        <213> Homo sapien

        <400> 99
```
gtggccgcgc gcaggtgttt cctcgtaccg cagggccccc tcccttcccc aggcgtccct      60
cggcgcctct gcgggcccga ggaggagcgg ctggcgggtg gggggagtgt gacccaccct      120
cggtgagaaa agccttctct agcgatctga gaggcgtgcc ttggggggtac c             171
```

        <210> 100
        <211> 269
        <212> DNA
        <213> Homo sapien

```
<400> 100
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc    60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc   120
aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga   180
cagccggaac agagcccggt gaagcgggag gcctcgggga gccctcgggg aagggcggcc   240
cgagagatac gcaggtgcag gtggccgcc                                     269


    <210> 101
    <211> 405
    <212> DNA
    <213> Homo sapien


    <400> 101
ttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca    60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg   120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaacgaagca aataacatgg   180
agtgggtgca ccctccctgt agaacctggt tacaaagctt ggggcagttc acctggtctg   240
tgaccgtcat tttcttgaca tcaatgttat tagaagtcag gatatctttt agagagtcca   300
ctgttctgga gggagattag ggtttcttgc caaatccaac aaaatccact gaaaaagttg   360
gatgatcagt acgaataccg aggcatattc tcatatcggt ggcca                  405


    <210> 102
    <211> 470
    <212> DNA
    <213> Homo sapien


    <400> 102
ttttttttt ttttttttt ttttttttt ttttttttt ttttttttt ttttttttt       60
ggcacttaat ccattttat ttcaaaatgt ctacaaattt aatcccatta tacggtattt   120
tcaaaatcta aattattcaa attagccaaa tccttaccaa ataatacccca aaaatcaaaa  180
atatacttct ttcagcaaac ttgttacata aattaaaaaa atatatacgg ctggtgtttt  240
caaagtacaa ttatcttaac actgcaaaca ttttaaggaa ctaaaataaa aaaaaacact  300
ccgcaaaggt taaagggaac aacaaattct tttacaacac cattataaaa atcatatctc  360
aaatcttagg ggaatatata cttcacacgg gatcttaact tttactcact ttgtttattt  420
ttttaaacca ttgtttgggc ccaacacaat ggaatccccc ctggactagt             470


    <210> 103
    <211> 581
    <212> DNA
    <213> Homo sapien


    <400> 103
ttttttttt ttttttttga ccccctctt ataaaaaaca agttaccatt ttattttact    60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac  120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt  180
gaaaatcttc tctagctctt ttgactgtaa attttttgact cttgtaaaac atccaaattc  240
.attttttcttg tctttaaaat tatctaatct ttccattttt tccctattcc aagtcaattt 300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa  360
agggaaaaca ggaagagaaa tggcacacaa aacaaacatt ttatattcat atttctacct  420
acgttaataa aatagcattt tgtgaagcca gctcaaaga aggcttagat cctttttatgt  480
ccatttttagt cactaaacga tatcaaagtg ccagaatgca aaaggtttgt gaacatttat  540
tcaaaagcta atataagata tttcacatac tcatctttct g                      581


    <210> 104
    <211> 578
    <212> DNA
    <213> Homo sapien
```

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        <400> 104
   tttttttttt   ttttttttttt   tttttctctt   cttttttttt   gaaatgagga   tcgagttttt        60
   cactctctag   atagggcatg   aagaaaactc   atctttccag   ctttaaaata   acaatcaaat       120
   ctcttatgct   atatcatatt   ttaagttaaa   ctaatgagtc   actggcttat   cttctcctga       180
   aggaaatctg   ttcattcttc   tcattcatat   agttatatca   agtactacct   tgcatattga       240
   gaggttttc   ttctctattt   acacatatat   ttccatgtga   atttgtatca   aacctttatt       300
   ttcatgcaaa   ctagaaaata   atgtttcttt   tgcataagag   aagagaacaa   tatagcatta       360
   caaaactgct   caaattgttt   gttaagttat   ccattataat   tagttggcag   gagctaatac       420
   aaatcacatt   tacgacagca   ataataaaac   tgaagtacca   gttaaatatc   caaaataatt       480
   aaaggaacat   ttttagcctg   ggtataatta   gctaattcac   tttacaagca   tttattagaa       540
   tgaattcaca   tgttattatt   cctagcccaa   cacaatgg                                   578


        <210> 105
        <211> 538
        <212> DNA
        <213> Homo sapien


        <400> 105
   tttttttttt   ttttttcagta   ataatcagaa   caatatttat   ttttatattt   aaaattcata       60
   gaaaagtgcc   ttacatttaa   taaaagtttg   tttctcaaag   tgatcagagg   aattagatat      120
   gtcttgaaca   ccaatattaa   tttgaggaaa   atacaccaaa   atacattaag   taaattatttt      180
   aagatcatag   agcttgtaag   tgaaaagata   aaatttgacc   tcagaaactc   tgagcattaa      240
   aaatccacta   ttagcaaata   aattactatg   gacttcttgc   tttaattttg   tgatgaatat      300
   ggggtgtcac   tggtaaacca   acacattctg   aaggatacat   tacttagtga   tagattctta  ·   360
   tgtactttgc   taatacgtgg   atatgagttg   acaagtttct   ctttcttcaa   tctttttaagg      420
   ggcgagaaat   gaggaagaaa   agaaaaggat   tacgcatact   gttctttcta   tggaaggatt      480
   agatatgttt   cctttgccaa   tattaaaaaa   ataataatgt   ttactactag   tgaaaccc   .    538


        <210> 106
        <211> 473
        <212> DNA
        <213> Homo sapien


        <400> 106
   tttttttttt   ttttttagtc   aagtttctat   ttttattata   attaaagtct   tggtcatttc        60
   atttattagc   tctgcaactt   acatatttaa   attaaagaaa   cgttttagac   aactgtacaa       120
   tttataaatg   taaggtgcca   ttattgagta   atatattcct   ccaagagtgg   atgtgtccct       180
   tctcccacca   actaatgaac   agcaacatta   gtttaatttt   attagtagat   atacactgct       240
   gcaaacgcta   attctcttct   ccatccccat   gtgatattgt   gtatatgtgt   gagttggtag       300
   aatgcatcac   aatctacaat   caacagcaag   atgaagctag   gctgggcttt   cggtgaaaat       360
   agactgtgtc   tgtctgaatc   aaatgatctg   acctatcctc   ggtggcaaga   actcttcgaa       420
   ccgcttcctc   aaaggcgctg   ccacatttgt   ggctctttgc   acttgtttca   aaa              473


        <210> 107
        <211> 1621
        <212> DNA
        <213> Homo sapien


        <400> 107
   cgccatggca   ctgcagggca   tctcggtcat   ggagctgtcc   ggcctggccc   cgggcccgtt        60
   ctgtgctatg   gtcctggctg   acttcggggc   gcgtgtggta   cgcgtggacc   ggcccggctc  ,    120
   ccgctacgac   gtgagccgct   tgggccgggg   caagcgctcg   ctagtgctgg   acctgaagca       180
   gccgcgggga   gccgccgtgc   tgcggcgtct   gtgcaagcgg   tcggatgtgc   tgctggagcc       240
   cttccgccgc   ggtgtcatgg   agaaactcca   gctgggccca   gagattctgc   agcgggaaaa       300
   tccaaggctt   atttatgcca   ggctgagtgg   atttggccag   tcaggaagct   tctgccggtt       360
   agctggccac   gatatcaact   atttggcttt   gtcaggtgtt   ctctcaaaaa   ttggcagaag       420
   tggtgagaat   ccgtatgccc   cgctgaatct   cctggctgac   tttgctggtg   gtggccttat       480
   gtgtgcactg   ggcattataa   tggctctttt   tgaccgcaca   cgcactgaca   agggtcaggt       540
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cattgatgca aatatggtgg aaggaacagc atatttaagt tcttttctgt ggaaaactca     600
gaaatcgagt ctgtgggaag cacctcgagg acagaacatg ttggatggtg gagcaccttt     660
ctatacgact tacaggacag cagatgggga attcatggct gttggagcaa tagaaccca     720
gttctacgag ctgctgatca aaggacttgg actaaagtct gatgaacttc ccaatcagat     780
gagcatggat gattggccag aaatgaagaa gaagtttgca gatgtatttg caaagaagac     840
gaaggcagag tggtgtcaaa tctttgacgg cacagatgcc tgtgtgactc cggttctgac     900
ttttgaggag gttgttcatc atgatcacaa caaggaacgg ggctcgttta tcaccagtga     960
ggagcaggac gtgagccccc gccctgcacc tctgctgtta aacaccccag ccatcccttc    1020
tttcaaaagg gatcctttca taggagaaca cactgaggag atacttgaag aatttggatt    1080
cagccgcgaa gagatttatc agcttaactc agataaaatc attgaaagta ataaggtaaa    1140
agctagtctc taacttccag gcccacggct caagtgaatt tgaatactgc atttacagtg    1200
tagagtaaca cataacattg tatgcatgga aacatggagg aacagtatta cagtgtccta    1260
ccactctaat caagaaaaga attacagact ctgattctac agtgatgatt gaattctaaa    1320
aatggttatc attagggctt ttgatttata aaactttggg tacttatact aaattatggt    1380
agttattctg ccttccagtt tgcttgatat atttgttgat attaagattc ttgacttata    1440
ttttgaatgg gttctagtga aaaaggaatg atatattctt gaagacatcg atatacattt    1500
atttacactc ttgattctac aatgtagaaa atgaggaaat gccacaaatt gtatggtgat    1560
aaaagtcacg tgaaacaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa    1620
a                                                                    1621
```

        <210> 108
        <211> 382
        <212> PRT
        <213> Homo sapien

        <400> 108
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Met Ala Leu Gln Gly Ile Ser Val Met Glu Leu Ser Gly Leu Ala Pro
1               5                   10                  15
Gly Pro Phe Cys Ala Met Val Leu Ala Asp Phe Gly Ala Arg Val Val
            20                  25                  30
Arg Val Asp Arg Pro Gly Ser Arg Tyr Asp Val Ser Arg Leu Gly Arg
        35                  40                  45
Gly Lys Arg Ser Leu Val Leu Asp Leu Lys Gln Pro Arg Gly Ala Ala
    50                  55                  60
Val Leu Arg Arg Leu Cys Lys Arg Ser Asp Val Leu Leu Glu Pro Phe
65                  70                  75                  80
Arg Arg Gly Val Met Glu Lys Leu Gln Leu Gly Pro Glu Ile Leu Gln
                85                  90                  95
Arg Glu Asn Pro Arg Leu Ile Tyr Ala Arg Leu Ser Gly Phe Gly Gln
            100                 105                 110
Ser Gly Ser Phe Cys Arg Leu Ala Gly His Asp Ile Asn Tyr Leu Ala
        115                 120                 125
Leu Ser Gly Val Leu Ser Lys Ile Gly Arg Ser Gly Glu Asn Pro Tyr
    130                 135                 140
Ala Pro Leu Asn Leu Leu Ala Asp Phe Ala Gly Gly Gly Leu Met Cys
145                 150                 155                 160
Ala Leu Gly Ile Ile Met Ala Leu Phe Asp Arg Thr Arg Thr Asp Lys
                165                 170                 175
Gly Gln Val Ile Asp Ala Asn Met Val Glu Gly Thr Ala Tyr Leu Ser
            180                 185                 190
Ser Phe Leu Trp Lys Thr Gln Lys Ser Ser Leu Trp Glu Ala Pro Arg
        195                 200                 205
Gly Gln Asn Met Leu Asp Gly Gly Ala Pro Phe Tyr Thr Thr Tyr Arg
    210                 215                 220
Thr Ala Asp Gly Glu Phe Met Ala Val Gly Ala Ile Glu Pro Gln Phe
225                 230                 235                 240
Tyr Glu Leu Leu Ile Lys Gly Leu Gly Leu Lys Ser Asp Glu Leu Pro
                245                 250                 255
```

```
Asn Gln Met Ser Met Asp Asp Trp Pro Glu Met Lys Lys Lys Phe Ala
            260             265             270
Asp Val Phe Ala Lys Lys Thr Lys Ala Glu Trp Cys Gln Ile Phe Asp
        275             280             285
Gly Thr Asp Ala Cys Val Thr Pro Val Leu Thr Phe Glu Glu Val Val
    290             295             300
His His Asp His Asn Lys Glu Arg Gly Ser Phe Ile Thr Ser Glu Glu
305             310             315             320
Gln Asp Val Ser Pro Arg Pro Ala Pro Leu Leu Leu Asn Thr Pro Ala
            325             330             335
Ile Pro Ser Phe Lys Arg Asp Pro Phe Ile Gly Glu His Thr Glu Glu
            340             345             350
Ile Leu Glu Glu Phe Gly Phe Ser Arg Glu Glu Ile Tyr Gln Leu Asn
        355             360             365
Ser Asp Lys Ile Ile Glu Ser Asn Lys Val Lys Ala Ser Leu
370                 375             380
```

```
            <210> 109
            <211> 1524
            <212> DNA
            <213> Homo sapien

            <400> 109
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gggcctggcc atgcctcact gagccagcgc ctgcgcctct acctcgccga cagctggaac       120
cagtgcgacc tagtggctct cacctgcttc ctcctgggcg tgggctgccg gctgaccccg       180
ggtttgtacc acctgggccg cactgtcctc tgcatcgact tcatggtttt cacggtgcgg       240
ctgcttcaca tcttcacggt caacaaacag ctggggccca agatcgtcat cgtgagcaag       300
atgatgaagg acgtgttctt cttcctcttc ttcctcggcg tgtggctggt agcctatggc       360
gtggccacgg aggggctcct gaggccacgg gacagtgact cccaagtat cctgcgccgc        420
gtcttctacc gtccctacct gcagatcttc gggcagattc cccaggagga catggacgtg       480
gccctcatgg agcacagcaa ctgctcgtcg gagcccggct ctgggcaca ccctcctggg        540
gcccaggcgg gcacctgcgt ctcccagtat gccaactggc tggtggtgct gctcctcgtc       600
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acattcggca agtacagggg caacagcgat ctctactgga aggcgcagcg ttaccgcctc       720
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cgcctcctgc tcaggcaatt gtgcaggcga ccccggagcc cccagccgtc ctccccggcc       840
ctcgagcatt tccgggttta cctttctaag gaagccgagc ggaagctgct aacgtgggaa       900
tcggtgcata aggagaactt tctgctggca cgcgctaggg acaagcggga gagcgactcc       960
gagcgtctga gcgcacgtc ccagaaggtg gacttggcac tgaaacagct gggacacatc       1020
cgcgagtacg aacagcgcct gaaagtgctg gagcgggagg tccagcagtg tagccgcgtc       1080
ctggggtggg tggccgaggc cctgagccgc tctgccttgc tgcccccagg tgggccgcca       1140
ccccctgacc tgcctgggtc caaagactga gccctgctgg cggacttcaa ggagaagccc       1200
ccacagggga ttttgctcct agagtaaggc tcatctgggc ctcggccccc gcacctggtg       1260
gccttgtcct tgaggtgagc cccatgtcca tctgggccac tgtcaggacc acctttggga       1320
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ggatcaaggc ctggatcccg gccgttatc catctggagg ctgcagggtc cttggggtaa       1440
cagggaccac agaccctca ccactcacag attcctcaca ctggggaaat aaagccattt        1500
cagaggaaaa aaaaaaaaaa aaaa                                               1524

            <210> 110
            <211> 3410
            <212> DNA
            <213> Homo sapien

            <400> 110
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gtgatgagac gtgtccccac tgaggtgccc cacagcagca ggtgttgagc atgggctgag       120
```

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aagctggacc ggcaccaaag ggctggcaga aatgggcgcc tggctgattc ctaggcagtt      180
ggcggcagca aggaggagag gccgcagctt ctggagcaga gccgagacga agcagttctg      240
gagtgcctga acggccccct gagccctacc cgcctggccc actatggtcc agaggctgtg      300
ggtgagccgc ctgctgcggc accggaaagc ccagctcttg ctggtcaacc tgctaacctt      360
tggcctggag gtgtgtttgg ccgcaggcat cacctatgtg ccgcctctgc tgctggaagt      420
gggggtagag gagaagttca tgaccatggt gctgggcatt ggtccagtgc tgggcctggt      480
ctgtgtcccg ctcctaggct cagccagtga ccactggcgt ggacgctatg ccgccgccg      540
gcccttcatc tgggcactgt ccttgggcat cctgctgagc ctctttctca tcccaagggc      600
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cctgggcgtg gggctgctgg acttctgtgg ccaggtgtgc ttcactccac tggaggccct      720
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catgatcagt cttgggggct gcctgggcta cctcctgcct gccattgact gggacaccag      840
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cgagccagca gaagggctgt cggcccccctc cttgtcgccc cactgctgtc catgccgggc     1020
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catgccccgc accctgcgcc ggctcttcgt ggctgagctg tgcagctgga tggcactcat     1140
gaccttcacg ctgttttaca cggatttcgt gggcgagggg ctgtaccagg gcgtgcccag     1200
agctgagccg ggcaccgagg cccggagaca ctatgatgaa ggcgttcgga tgggcagcct     1260
ggggctgttc ctgcagtgcg ccatctccct ggtcttctct ctggtcatgg accggctggt     1320
gcagcgattc ggcactcgag cagtctattt ggccagtgtg gcagctttcc ctgtggctgc     1380
cggtgccaca tgcctgtccc acagtgtggc cgtggtgaca gcttcagccg ccctcaccgg     1440
gttcaccttc tcagccctgc agatcctgcc ctacacactg gcctccctct accaccggga     1500
gaagcaggtg ttcctgccca ataccgagg ggacactgga ggtgctagca gtgaggacag     1560
cctgatgacc agcttcctgc caggccctaa gcctggagct cccttcccta atggacacgt     1620
gggtgctgga ggcagtggcc tgctcccacc tccacccgcg ctctgcgggg cctctgcctg     1680
tgatgtctcc gtacgtgtgg tggtggggtga gcccaccgag gccagggtgg ttccgggccg     1740
gggcatctgc ctggacctcg ccatcctgga tagtgccttc ctgctgtccc aggtggcccc     1800
atccctgttt atgggctcca ttgtccagct cagccagtct gtcactgcct atatggtgtc     1860
tgccgcaggc ctgggtctgg tcgccattta ctttgctaca caggtagtat ttgacaagag     1920
cgacttggcc aaatactcag cgtagaaaac ttccagcaca ttggggtgga gggcctgcct     1980
cactgggtcc cagctccccg ctcctgttag ccccatgggg ctgccgggct ggccgccagt     2040
ttctgttgct gccaaagtaa tgtggctctc tgctgccacc ctgtgctgct gaggtgcgta     2100
gctgcacagc tgggggctgg ggcgtccctc tcctctctcc ccagtctcta gggctgcctg     2160
actggaggcc ttccaagggg gtttcagtct ggacttatac agggaggcca gaaggggctcc     2220
atgcactgga atgcggggac tctgcaggtg gattacccag gctcagggtt aacagctagc     2280
ctcctagttg agacacacct agagaagggt ttttgggagc tgaataaact cagtcacctg     2340
gtttcccatc tctaagcccc ttaacctgca gcttcgttta atgtagctct tgcatgggag     2400
tttctaggat gaaacactcc tccatgggat ttgaacatat gacttatttg taggggaaga     2460
gtcctgaggg gcaacacaca agaaccaggt cccctcagcc cacagcactg tctttttgct     2520
gatccaccc cctcttacct tttatcagga tgtggcctgt tggtccttct gttgccatca     2580
cagagacaca ggcatttaaa tatttaactt atttatttaa caaagtagaa gggaatccat     2640
tgctagcttt tctgtgttgg tgtctaatat ttgggtaggg tgggggatcc ccaacaatca     2700
ggtcccctga gatagctggt cattgggctg atcattgcca gaatcttctt ctcctggggt     2760
ctggccccc aaaatgccta acccaggacc ttggaaattc tactcatccc aaatgataat     2820
tccaaatgct gttacccaag gttagggtgt tgaaggaagg tagagggtgg ggcttcaggt     2880
ctcaacggct tccctaacca cccctcttct cttggcccag cctggttccc cccacttcca     2940
ctccctcta ctctctctag gactgggctg atgaaggcac tgccaaaat ttcccctacc      3000
cccaactttc ccctaccccc aactttcccc accagctcca caaccctgtt tggagctact     3060
gcaggaccag aagcacaaag tgcggtttcc caagcctttg tccatctcag cccccagagt     3120
atatctgtgc ttggggaatc tcacacagaa actcaggagc acccctgcc tgagctaagg     3180
gaggtcttat ctctcagggg gggtttaagt gccgtttgca ataatgtcgt cttatttatt     3240
tagcggggtg aatatttat actgtaagtg agcaatcaga gtataatgtt tatggtgaca     3300
aaattaaagg ctttcttata tgtttaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa     3360
aaaaaaaara aaaaaaaaaa aaaaaaaaaa aaaaaaataa aaaaaaaaa             3410
```

<210> 111
<211> 1289

```
        <212> DNA
        <213> Homo sapien

        <400> 111
agccaggcgt ccctctgcct gcccactcag tggcaacacc cgggagctgt tttgtccttt      60
gtggagcctc agcagttccc tctttcagaa ctcactgcca agagccctga acaggagcca     120
ccatgcagtg cttcagcttc attaagacca tgatgatcct cttcaatttg ctcatctttc     180
tgtgtggtgc agccctgttg gcagtgggca tctgggtgtc aatcgatggg gcatcctttc     240
tgaagatctt cgggccactg tcgtccagtg ccatgcagtt tgtcaacgtg ggctacttcc     300
tcatcgcagc cggcgttgtg gtctttgctc ttggtttcct gggctgctat ggtgctaaga     360
ctgagagcaa gtgtgccctc gtgacgttct tcttcatcct cctcctcatc ttcattgctg     420
aggttgcagc tgctgtggtc gccttggtgt acaccacaat ggctgagcac ttcctgacgt     480
tgctggtagt gcctgccatc aagaaagatt atggttccca ggaagacttc actcaagtgt     540
ggaacaccac catgaaaggg ctcaagtgct gtggcttcac caactatacg gattttgagg     600
actcacccta cttcaaagag aacagtgcct tcccccatt ctgttgcaat gacaacgtca     660
ccaacacagc caatgaaacc tgcaccaagc aaaaggctca cgaccaaaaa gtagagggtt     720
gcttcaatca gcttttgtat gacatccgaa ctaatgcagt caccgtgggt ggtgtggcag     780
ctggaattgg gggcctcgag ctggctgcca tgattgtgtc catgtatctg tactgcaatc     840
tacaataagt ccacttctgc ctctgccact actgctgcca catgggaact gtgaagaggc     900
accctggcaa gcagcagtga ttggggggagg ggacaggatc taacaatgtc acttgggcca     960
gaatggacct gccctttctg ctccagactt ggggctagat agggaccact cctttagcg     1020
atgcctgact ttccttccat tggtgggtgg atgggtgggg ggcattccag agcctctaag    1080
gtagccagtt ctgttgccca ttcccccagt ctattaaacc cttgatatgc cccctaggcc    1140
tagtggtgat cccagtgctc tactggggga tgagagaaag gcattttata gcctgggcat    1200
aagtgaaatc agcagagcct ctgggtggat gtgtagaagg cacttcaaaa tgcataaacc    1260
tgttacaatg ttaaaaaaaa aaaaaaaaa                                      1289

        <210> 112
        <211> 315
        <212> PRT
        <213> Homo sapien

        <400> 112
Met Val Phe Thr Val Arg Leu Leu His Ile Phe Thr Val Asn Lys Gln
1               5                   10                  15
Leu Gly Pro Lys Ile Val Ile Val Ser Lys Met Met Lys Asp Val Phe
            20                  25                  30
Phe Phe Leu Phe Phe Leu Gly Val Trp Leu Val Ala Tyr Gly Val Ala
        35                  40                  45
Thr Glu Gly Leu Leu Arg Pro Arg Asp Ser Asp Phe Pro Ser Ile Leu
    50                  55                  60
Arg Arg Val Phe Tyr Arg Pro Tyr Leu Gln Ile Phe Gly Gln Ile Pro
65                  70                  75                  80
Gln Glu Asp Met Asp Val Ala Leu Met Glu His Ser Asn Cys Ser Ser
                85                  90                  95
Glu Pro Gly Phe Trp Ala His Pro Pro Gly Ala Gln Ala Gly Thr Cys
            100                 105                 110
Val Ser Gln Tyr Ala Asn Trp Leu Val Val Leu Leu Leu Val Ile Phe
        115                 120                 125
Leu Leu Val Ala Asn Ile Leu Leu Val Asn Leu Leu Ile Ala Met Phe
    130                 135                 140
Ser Tyr Thr Phe Gly Lys Val Gln Gly Asn Ser Asp Leu Tyr Trp Lys
145                 150                 155                 160
Ala Gln Arg Tyr Arg Leu Ile Arg Glu Phe His Ser Arg Pro Ala Leu
                165                 170                 175
Ala Pro Pro Phe Ile Val Ile Ser His Leu Arg Leu Leu Leu Arg Gln
            180                 185                 190
Leu Cys Arg Arg Pro Arg Ser Pro Gln Pro Ser Ser Pro Ala Leu Glu
```

```
                     195                    200                    205
His Phe Arg Val Tyr Leu Ser Lys Glu Ala Glu Arg Lys Leu Leu Thr
    210                    215                    220
Trp Glu Ser Val His Lys Glu Asn Phe Leu Leu Ala Arg Ala Arg Asp
225                    230                    235                    240
Lys Arg Glu Ser Asp Ser Glu Arg Leu Lys Arg Thr Ser Gln Lys Val
                     245                    250                    255
Asp Leu Ala Leu Lys Gln Leu Gly His Ile Arg Glu Tyr Glu Gln Arg
                     260                    265                    270
Leu Lys Val Leu Glu Arg Glu Val Gln Gln Cys Ser Arg Val Leu Gly
                     275                    280                    285
Trp Val Ala Glu Ala Leu Ser Arg Ser Ala Leu Leu Pro Pro Gly Gly
                     290                    295                    300
Pro Pro Pro Pro Asp Leu Pro Gly Ser Lys Asp
305                    310                    315
```

<210> 113
<211> 553
<212> PRT
<213> Homo sapien

<400> 113
```
Met Val Gln Arg Leu Trp Val Ser Arg Leu Leu Arg His Arg Lys Ala
1                   5                    10                   15
Gln Leu Leu Leu Val Asn Leu Leu Thr Phe Gly Leu Glu Val Cys Leu
                    20                   25                   30
Ala Ala Gly Ile Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val
            35                   40                   45
Glu Glu Lys Phe Met Thr Met Val Leu Gly Ile Gly Pro Val Leu Gly
    50                   55                   60
Leu Val Cys Val Pro Leu Leu Gly Ser Ala Ser Asp His Trp Arg Gly
65                   70                   75                   80
Arg Tyr Gly Arg Arg Arg Pro Phe Ile Trp Ala Leu Ser Leu Gly Ile
                    85                   90                   95
Leu Leu Ser Leu Phe Leu Ile Pro Arg Ala Gly Trp Leu Ala Gly Leu
                    100                  105                  110
Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu Ala Leu Leu Ile Leu Gly
            115                  120                  125
Val Gly Leu Leu Asp Phe Cys Gly Gln Val Cys Phe Thr Pro Leu Glu
    130                  135                  140
Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg Gln Ala
145                  150                  155                  160
Tyr Ser Val Tyr Ala Phe Met Ile Ser Leu Gly Gly Cys Leu Gly Tyr
                    165                  170                  175
Leu Leu Pro Ala Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu
                    180                  185                  190
Gly Thr Gln Glu Glu Cys Leu Phe Gly Leu Leu Thr Leu Ile Phe Leu
            195                  200                  205
Thr Cys Val Ala Ala Thr Leu Leu Val Ala Glu Glu Ala Ala Leu Gly
    210                  215                  220
Pro Thr Glu Pro Ala Glu Gly Leu Ser Ala Pro Ser Leu Ser Pro His
225                  230                  235                  240
Cys Cys Pro Cys Arg Ala Arg Leu Ala Phe Arg Asn Leu Gly Ala Leu
                    245                  250                  255
Leu Pro Arg Leu His Gln Leu Cys Cys Arg Met Pro Arg Thr Leu Arg
            260                  265                  270
Arg Leu Phe Val Ala Glu Leu Cys Ser Trp Met Ala Leu Met Thr Phe
            275                  280                  285
```

```
Thr Leu Phe Tyr Thr Asp Phe Val Gly Glu Gly Leu Tyr Gln Gly Val
    290             295             300
Pro Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
305             310             315             320
Val Arg Met Gly Ser Leu Gly Leu Phe Leu Gln Cys Ala Ile Ser Leu
            325             330             335
Val Phe Ser Leu Val Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg
            340             345             350
Ala Val Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala
        355             360             365
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
    370             375             380
Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr Leu Ala
385             390             395             400
Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro Lys Tyr Arg Gly
            405             410             415
Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser Leu Met Thr Ser Phe Leu
        420             425             430
Pro Gly Pro Lys Pro Gly Ala Pro Phe Pro Asn Gly His Val Gly Ala
    435             440             445
Gly Gly Ser Gly Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser
    450             455             460
Ala Cys Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala
465             470             475             480
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
            485             490             495
Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met Gly Ser
            500             505             510
Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met Val Ser Ala Ala
    515             520             525
Gly Leu Gly Leu Val Ala Ile Tyr Phe Ala Thr Gln Val Val Phe Asp
    530             535             540
Lys Ser Asp Leu Ala Lys Tyr Ser Ala
545             550
```

```
        <210> 114
        <211> 241
        <212> PRT
        <213> Homo sapien

        <400> 114
Met Gln Cys Phe Ser Phe Ile Lys Thr Met Met Ile Leu Phe Asn Leu
1           5               10              15
Leu Ile Phe Leu Cys Gly Ala Ala Leu Leu Ala Val Gly Ile Trp Val
            20              25              30
Ser Ile Asp Gly Ala Ser Phe Leu Lys Ile Phe Gly Pro Leu Ser Ser
        35              40              45
Ser Ala Met Gln Phe Val Asn Val Gly Tyr Phe Leu Ile Ala Ala Gly
    50              55              60
Val Val Val Phe Ala Leu Gly Phe Leu Gly Cys Tyr Gly Ala Lys Thr
65              70              75              80
Glu Ser Lys Cys Ala Leu Val Thr Phe Phe Phe Ile Leu Leu Leu Ile
            85              90              95
Phe Ile Ala Glu Val Ala Ala Ala Val Val Ala Leu Val Tyr Thr Thr
            100             105             110
Met Ala Glu His Phe Leu Thr Leu Leu Val Val Pro Ala Ile Lys Lys
    115             120             125
Asp Tyr Gly Ser Gln Glu Asp Phe Thr Gln Val Trp Asn Thr Thr Met
```

44

```
        130                  135                  140
Lys Gly Leu Lys Cys Cys Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp
145                      150                  155                  160
Ser Pro Tyr Phe Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn
                165                  170                  175
Asp Asn Val Thr Asn Thr Ala Asn Glu Thr Cys Thr Lys Gln Lys Ala
                180                  185                  190
His Asp Gln Lys Val Glu Gly Cys Phe Asn Gln Leu Leu Tyr Asp Ile
        195                  200                  205
Arg Thr Asn Ala Val Thr Val Gly Gly Val Ala Ala Gly Ile Gly Gly
        210                  215                  220
Leu Glu Leu Ala Ala Met Ile Val Ser Met Tyr Leu Tyr Cys Asn Leu
225                      230                  235                  240
Gln
```

```
        <210> 115
        <211> 366
        <212> DNA
        <213> Homo sapien


        <400> 115
gctctttctc tcccctcctc tgaatttaat tctttcaact tgcaatttgc aaggattaca        60
catttcactg tgatgtatat tgtgttgcaa aaaaaaaaaa gtgtctttgt ttaaaattac       120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga       180
actggtagaa aaacatctga agagctagtc tatcagcatc tgacaggtga attggatggt       240
tctcagaacc atttcaccca dacagcctgt ttctatcctg tttaataaat tagtttgggt       300
tctctacatg cataacaaac cctgctccaa tctgtcacat aaaagtctgt gacttgaagt       360
ttagtc                                                                   366
```

```
        <210> 116
        <211> 282
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(282)
        <223> n = A,T,C or G


        <400> 116
acaaagatga accatttcct atattatagc aaaattaaaa tctacccgta ttctaatatt        60
gagaaatgag atnaaacaca atnttataaa gtctacttag agaagatcaa gtgacctcaa       120
agactttact attttcatat tttaagacac atgatttatc ctattttagt aacctggttc       180
atacgttaaa caaaggataa tgtgaacagc agagaggatt tgttggcaga aaatctatgt       240
tcaatctnga actatctana tcacagacat ttctattcct tt                          282
```

```
        <210> 117
        <211> 305
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(305)
        <223> n = A,T,C or G


        <400> 117
```

```
acacatgtcg cttcactgcc ttcttagatg cttctggtca acatanagga acagggacca      60
tatttatcct ccctcctgaa acaattgcaa aataanacaa aatatatgaa acaattgcaa     120
aataaggcaa aatatatgaa acaacaggtc tcgagatatt ggaaatcagt caatgaagga     180
tactgatccc tgatcactgt cctaatgcag gatgtgggaa acagatgagg tcacctctgt     240
gactgcccca gcttactgcc tgtagagagt ttctangctg cagttcagac agggagaaat     300
tgggt                                                                 305
```

```
        <210> 118
        <211> 71
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(71)
        <223> n = A,T,C or G


        <400> 118
accaaggtgt ntgaatctct gacgtgggga tctctgattc ccgcacaatc tgagtggaaa      60
aantcctggg t                                                           71
```

```
        <210> 119
        <211> 212
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(212)
        <223> n = A,T,C or G


        <400> 119
actccggttg gtgtcagcag cacgtggcat tgaacatngc aatgtggagc ccaaaccaca      60
gaaaatgggg tgaaattggc caactttcta tnaacttatg ttggcaanтt tgccaccaac     120
agtaagctgg cccttctaat aaaagaaaat tgaaaggttt ctcactaanc ggaattaant     180
aatggantca aganactccc aggcctcagc gt                                   212
```

```
        <210> 120
        <211> 90
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(90)
        <223> n = A,T,C or G


        <400> 120
actcgttgca natcaggggc cccccagagt caccgttgca ggagtccttc tggtcttgcc      60
ctccgccggc gcagaacatg ctggggtggt                                       90
```

```
        <210> 121
        <211> 218
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
```

```
      <222> (1)...(218)
      <223> n = A,T,C or G

      <400> 121
tgtancgtga anacgacaga nagggttgtc aaaaatggag aanccttgaa gtcattttga       60
gaataagatt tgctaaaaga tttggggcta aaacatggtt attgggagac atttctgaag       120
atatncangt aaattangga atgaattcat ggttcttttg ggaattcctt tacgatngcc       180
agcatanact tcatgtgggg atancagcta cccttgta                               218


      <210> 122
      <211> 171
      <212> DNA
      <213> Homo sapien

      <400> 122
taggggtgta tgcaactgta aggacaaaaa ttgagactca actggcttaa ccaataaagg       60
catttgttag ctcatggaac aggaagtcgg atggtggggc atcttcagtg ctgcatgagt       120
caccacccccg gcggggtcat ctgtgccaca ggtccctgtt gacagtgcgg t              171


      <210> 123
      <211> 76
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(76)
      <223> n = A,T,C or G

      <400> 123
tgtagcgtga agacnacaga atggtgtgtg ctgtgctatc caggaacaca tttattatca       60
ttatcaanta ttgtgt                                                      76


      <210> 124
      <211> 131
      <212> DNA
      <213> Homo sapien

      <400> 124
acctttcccc aaggccaatg tcctgtgtgc taactggccg gctgcaggac agctgcaatt       60
caatgtgctg ggtcatatgg aggggaggag actctaaaat agccaatttt attctcttgg       120
ttaagatttg t                                                          131


      <210> 125
      <211> 432
      <212> DNA
      <213> Homo sapien

      <400> 125
actttatcta ctggctatga aatagatggt ggaaaattgc gttaccaact ataccactgg       60
cttgaaaaag aggtgatagc tcttcagagg acttgtgact tttgctcaga tgctgaagaa       120
ctacagtctg catttggcag aaatgaagat gaatttggat taaatgagga tgctgaagat       180
ttgcctcacc aaacaaaagt gaaacaactg agagaaaatt ttcaggaaaa aagacagtgg       240
ctcttgaagt atcagtcact tttgagaatg tttcttagtt actgcatact tcatggatcc       300
catggtgggg tcttgcatc tgtaagaatg gaattgattt tgcttttgca agaatctcag       360
caggaaacat cagaaccact attttctagc cctctgtcag agcaaacctc agtgcctctc       420
ctctttgctt gt                                                          432
```

47

```
        <210> 126
        <211> 112
        <212> DNA
        <213> Homo sapien

        <400> 126
acacaacttg aatagtaaaa tagaaactga gctgaaattt ctaattcact ttctaaccat        60
agtaagaatg atatttcccc ccagggatca ccaaatattt ataaaaattt gt               112

        <210> 127
        <211> 54
        <212> DNA
        <213> Homo sapien

        <400> 127
accacgaaac cacaaacaag atggaagcat caatccactt gccaagcaca gcag             54

        <210> 128
        <211> 323
        <212> DNA
        <213> Homo sapien

        <400> 128
acctcattag taattgtttt gttgtttcat ttttttctaa tgtctcccct ctaccagctc       60
acctgagata acagaatgaa aatggaagga cagccagatt tctcctttgc tctctgctca       120
ttctctctga agtctaggtt acccattttg gggacccatt ataggcaata aacacagttc       180
ccaaagcatt tggacagttt cttgttgtgt tttagaatgg ttttcctttt tcttagcctt       240
ttcctgcaaa aggctcactc agtcccttgc ttgctcagtg gactgggctc cccagggcct       300
aggctgcctt ctttttccatg tcc                                              323

        <210> 129
        <211> 192
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(192)
        <223> n = A,T,C or G

        <400> 129
acatacatgt gtgtatattt ttaaatatca cttttgtatc actctgactt tttagcatac       60
tgaaaacaca ctaacataat ttntgtgaac catgatcaga tacaacccaa atcattcatc       120
tagcacattc atctgtgata naaagatagg tgagtttcat ttccttcacg ttggccaatg       180
gataaacaaa gt                                                           192

        <210> 130
        <211> 362
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(362)
        <223> n = A,T,C or G

        <400> 130
cccttttta tggaatgagt agactgtatg tttgaanatt tanccacaac ctctttgaca        60
```

```
tataatgacg caacaaaaag gtgctgttta gtcctatggt tcagtttatg cccctgacaa    120
gtttccattg tgttttgccg atcttctggc taatcgtggt atcctccatg ttattagtaa    180
ttctgtattc cattttgtta acgcctggta gatgtaacct gctangaggc taactttata    240
cttatttaaa agctcttatt ttgtggtcat taaaatggca atttatgtgc agcactttat    300
tgcagcagga agcacgtgtg ggttggttgt aaagctcttt gctaatctta aaaagtaatg    360
gg                                                                   362
```

        <210> 131
        <211> 332
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(332)
        <223> n = A,T,C or G

        <400> 131
```
cttttttgaaa gatcgtgtcc actcctgtgg acatcttgtt ttaatggagt ttcccatgca    60
gtangactgg tatggttgca gctgtccaga taaaaacatt tgaagagctc caaaatgaga    120
gttctcccag gttcgccctg ctgctccaag tctcagcagc agcctctttt aggaggcatc    180
ttctgaacta gattaaggca gcttgtaaat ctgatgtgat ttggtttatt atccaactaa    240
cttccatctg ttatcactgg agaaagccca gactccccan gacnggtacg gattgtgggc    300
atanaaggat tgggtgaagc tggcgttgtg gt                                  332
```

        <210> 132
        <211> 322
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(322)
        <223> n = A,T,C or G

        <400> 132
```
acttttgcca ttttgtatat ataaacaatc ttgggacatt ctcctgaaaa ctaggtgtcc    60
agtggctaag agaactcgat ttcaagcaat tctgaaagga aaaccagcat gacacagaat    120
ctcaaattcc caaacagggg ctctgtggga aaaatgaggg aggacctttg tatctcgggt    180
tttagcaagt taaaatgaan atgacaggaa aggcttattt atcaacaaag agaagagttg    240
ggatgcttct aaaaaaaact ttggtagaga aaataggaat gctnaatcct agggaagcct    300
gtaacaatct acaattggtc ca                                            322
```

        <210> 133
        <211> 278
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(278)
        <223> n = A,T,C or G

        <400> 133
```
acaagccttc acaagtttaa ctaaattggg attaatcttt ctgtanttat ctgcataatt    60
cttgtttttc tttccatctg gctcctgggt tgacaatttg tggaaacaac tctattgcta    120
ctatttaaaa aaaatcacaa atctttccct ttaagctatg ttnaattcaa actattcctg    180
ctattcctgt tttgtcaaag aaattatatt tttcaaaata tgtntatttg tttgatgggt    240
```

```
cccacgaaac actaataaaa accacagaga ccagcctg                                  278


        <210> 134
        <211> 121
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(121)
        <223> n = A,T,C or G

        <400> 134
gtttanaaaa cttgtttagc tccatagagg aaagaatgtt aaactttgta ttttaaaaca          60
tgattctctg aggttaaact tggttttcaa atgttatttt tacttgtatt ttgctttttgg        120
t                                                                         121


        <210> 135
        <211> 350
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(350)
        <223> n = A,T,C or G

        <400> 135
acttanaacc atgcctagca catcagaatc cctcaaagaa catcagtata atcctatacc          60
atancaagtg gtgactggtt aagcgtgcga caaaggtcag ctggcacatt acttgtgtgc        120
aaacttgata ctttttgttct aagtaggaac tagtatacag tncctaggan tggtactcca       180
gggtgccccc caactcctgc agccgctcct ctgtgccagn ccctgnaagg aactttcgct        240
ccacctcaat caagccctgg gccatgctac ctgcaattgg ctgaacaaac gtttgctgag        300
ttcccaagga tgcaaagcct ggtgctcaac tcctggggcg tcaactcagt                   350


        <210> 136
        <211> 399
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(399)
        <223> n = A,T,C or G

        <400> 136
tgtaccgtga agacgacaga agttgcatgg cagggacagg gcagggccga ggccagggtt          60
gctgtgattg tatccgaata ntcctcgtga gaaaagataa tgagatgacg tgagcagcct        120
gcagacttgt gtctgccttc aanaagccag acaggaaggc cctgcctgcc ttggctctga        180
cctggcggcc agccagccag ccacaggtgg gcttcttcct tttgtggtga caacnccaag        240
aaaactgcag aggcccaggg tcaggtgtna gtgggtangt gaccataaaa caccaggtgc        300
tcccaggaac ccgggcaaag gccatcccca cctacagcca gcatgcccac tggcgtgatg        360
ggtgcagang gatgaagcag ccagntgttc tgctgtggt                               399


        <210> 137
        <211> 165
        <212> DNA
        <213> Homo sapien
```

```
        <220>
        <221> misc_feature
        <222> (1)...(165)
        <223> n = A,T,C or G

        <400> 137
actggtgtgg tnggggggtga tgctggtggt anaagttgan gtgacttcan gatggtgtgt          60
ggaggaagtg tgtgaacgta gggatgtaga ngttttggcc gtgctaaatg agcttcggga         120
ttggctggtc ccactggtgg tcactgtcat tggtgggggtt cctgt                        165


        <210> 138
        <211> 338
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(338)
        <223> n = A,T,C or G

        <400> 138
actcactgga atgccacatt cacaacagaa tcagaggtct gtgaaaacat taatggctcc          60
ttaacttctc cagtaagaat cagggacttg aaatggaaac gttaacagcc acatgcccaa         120
tgctgggcag tctcccatgc cttccacagt gaaagggctt gagaaaaatc acatccaatg         180
tcatgtgttt ccagccacac caaaaggtgc ttggggtgga gggctggggg catananggt         240
cangcctcag gaagcctcaa gttccattca gctttgccac tgtacattcc ccatntttaa         300
aaaaactgat gcctttttt ttttttttttg taaaattc                                 338


        <210> 139
        <211> 382
        <212> DNA
        <213> Homo sapien

        <400> 139
gggaatcttg gtttttggca tctggtttgc ctatagccga ggccactttg acagaacaaa          60
gaaagggact tcgagtaaga aggtgattta cagccagcct agtgcccgaa gtgaaggaga         120
attcaaacag acctcgtcat tcctggtgtg agcctggtcg gctcaccgcc tatcatctgc         180
atttgcctta ctcaggtgct accggactct ggcccctgat gtctgtagtt tcacaggatg         240
ccttatttgt cttctacacc ccacagggcc ccctacttct tcggatgtgt ttttaataat         300
gtcagctatg tgccccatcc tccttcatgc cctccctccc tttcctacca ctgctgagtg         360
gcctggaact tgtttaaagt gt                                                   382


        <210> 140
        <211> 200
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(200)
        <223> n = A,T,C or G

        <400> 140
accaaanctt ctttctgttg tgttngattt tactataggg gtttngcttn ttctaaanat          60
acttttcatt taacancttt tgttaagtgt caggctgcac tttgctccat anaattattg         120
ttttcacatt tcaacttgta tgtgtttgtc tcttanagca ttggtgaaat cacatatttt         180
atattcagca taaaggagaa                                                      200
```

```
<210> 141
<211> 335
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(335)
<223> n = A,T,C or G

<400> 141
actttatttt caaaacactc atatgttgca aaaaacacat agaaaaataa agtttggtgg      60
gggtgctgac taaacttcaa gtcacagact tttatgtgac agattggagc agggtttgtt     120
atgcatgtag agaacccaaa ctaatttatt aaacaggata gaaacaggct gtctgggtga     180
aatggttctg agaaccatcc aattcacctg tcagatgctg atanactagc tcttcagatg     240
tttttctacc agttcagaga tnggttaatg actanttcca atggggaaaa agcaagatgg     300
attcacaaac caagtaattt taaacaaaga cactt                               335


<210> 142
<211> 459
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(459)
<223> n = A,T,C or G

<400> 142
accaggttaa tattgccaca tatatccttt ccaattgcgg gctaaacaga cgtgtattta      60
gggttgttta aagacaaccc agcttaatat caagagaaat tgtgaccttt catggagtat     120
ctgatggaga aaacactgag ttttgacaaa tcttatttta ttcagatagc agtctgatca     180
cacatggtcc aacaacactc aaataataaa tcaaatatna tcagatgtta aagattggtc     240
ttcaaacatc atagccaatg atgccccgct tgcctataat ctctccgaca taaaaccaca     300
tcaacacctc agtggccacc aaaccattca gcacagcttc cttaactgtg agctgtttga     360
agctaccagt ctgagcacta ttgactatnt ttttcangct ctgaatagct ctagggatct     420
cagcangggt gggaggaacc agctcaacct tggcgtant                          459


<210> 143
<211> 140
<212> DNA
<213> Homo sapien

<400> 143
acatttcctt ccaccaagtc aggactcctg gcttctgtgg gagttcttat cacctgaggg      60
aaatccaaac agtctctcct agaaaggaat agtgtcacca accccaccca tctccctgag     120
accatccgac ttccctgtgt                                               140


<210> 144
<211> 164
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(164)
<223> n = A,T,C or G
```

```
        <400> 144
acttcagtaa caacatacaa taacaacatt aagtgtatat tgccatcttt gtcattttct        60
atctatacca ctctcccttc tgaaaacaan aatcactanc caatcactta tacaaatttg       120
aggcaattaa tccatatttg ttttcaataa ggaaaaaaag atgt                        164


        <210> 145
        <211> 303
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(303)
        <223> n = A,T,C or G


        <400> 145
acgtagacca tccaactttg tatttgtaat ggcaaacatc cagnagcaat tcctaaacaa        60
actggagggt atttatcccc aattatccca ttcattaaca tgccctcctc ctcaggctat       120
gcaggacagc tatcataagt cggcccaggc atccagatac taccatttgt ataaacttca       180
gtaggggagt ccatccaagt gacaggtcta atcaaaggag gaaatggaac ataagcccag       240
tagtaaaatn ttgcttagct gaaacagcca caaaagactt accgccgtgg tgattaccat       300
caa                                                                     303


        <210> 146
        <211> 327
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(327)
        <223> n = A,T,C or G


        <400> 146
actgcagctc aattagaagt ggtctctgac tttcatcanc ttctccctgg gctccatgac        60
actggcctgg agtgactcat tgctctggtt ggttgagaga gctcctttgc caacaggcct       120
ccaagtcagg gctgggattt gtttcctttc cacattctag caacaatatg ctggccactt       180
cctgaacagg gagggtggga ggagccagca tggaacaagc tgccactttc taaagtagcc       240
agacttgccc ctgggcctgt cacacctact gatgaccttc tgtgcctgca ggatggaatg       300
taggggtgag ctgtgtgact ctatggt                                           327


        <210> 147
        <211> 173
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(173)
        <223> n = A,T,C or G


        <400> 147
acattgtttt tttgagataa agcattgana gagctctcct taacgtgaca caatggaagg        60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt       120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gtt             173


        <210> 148
```

```
        <211> 477
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(477)
        <223> n = A,T,C or G

        <400> 148
acaaccactt tatctcatcg aatttttaac ccaaactcac tcactgtgcc tttctatcct       60
atgggatata ttatttgatg ctccatttca tcacacatat atgaataata cactcatact      120
gccctactac ctgctgcaat aatcacattc ccttcctgtc ctgaccctga agccattggg      180
gtggtcctag tggccatcag tccangcctg caccttgagc ccttgagctc cattgctcac      240
nccancccac ctcaccgacc ccatcctctt acacagctac ctccttgctc tctaacccca      300
tagattatnt ccaaattcag tcaattaagt tactattaac actctacccg acatgtccag      360
caccactggt aagccttctc cagccaacac acacacacac acacncacac acacacatat      420
ccaggcacag gctacctcat cttcacaatc acccctttaa ttaccatgct atggtgg         477

        <210> 149
        <211> 207
        <212> DNA
        <213> Homo sapien

        <400> 149
acagttgtat tataatatca agaaataaac ttgcaatgag agcatttaag agggaagaac       60
taacgtattt tagagagcca aggaaggttt ctgtggggag tgggatgtaa ggtggggcct      120
gatgataaat aagagtcagc caggtaagtg ggtggtgtgg tatgggcaca gtgaagaaca      180
tttcaggcag agggaacagc agtgaaa                                          207

        <210> 150
        <211> 111
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(111)
        <223> n = A,T,C or G

        <400> 150
accttgattt cattgctgct ctgatggaaa cccaactatc taatttagct aaaacatggg       60
cacttaaatg tggtcagtgt ttggacttgt taactantgg catctttggg t              111

        <210> 151
        <211> 196
        <212> DNA
        <213> Homo sapien

        <400> 151
agcgcggcag gtcatattga acattccaga tacctatcat tactcgatgc tgttgataac       60
agcaagatgg ctttgaactc agggtcacca ccagctattg gaccttacta tgaaaaccat      120
ggataccaac cggaaaaccc ctatcccgca cagcccactg tggtccccac tgtctacgag      180
gtgcatccgg ctcagt                                                     196

        <210> 152
        <211> 132
        <212> DNA
```

```
      <213> Homo sapien

      <400> 152
acagcacttt cacatgtaag aagggagaaa ttcctaaatg taggagaaag ataacagaac      60
cttccccttt tcatctagtg gtggaaacct gatgctttat gttgacagga atagaaccag     120
gagggagttt gt                                                         132


      <210> 153
      <211> 285
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(285)
      <223> n = A,T,C or G

      <400> 153
acaanaccca nganaggcca ctggccgtgg tgtcatggcc tccaaacatg aaagtgtcag      60
cttctgctct tatgtcctca tctgacaact ctttaccatt tttatcctcg ctcagcagga     120
gcacatcaat aaagtccaaa gtcttggact tggccttggc ttggaggaag tcatcaacac     180
cctggctagt gagggtgcgg cgccgctcct ggatgacggc atctgtgaag tcgtgcacca     240
gtctgcaggc cctgtggaag cgccgtccac acggagtnag gaatt                     285


      <210> 154
      <211> 333
      <212> DNA
      <213> Homo sapien

      <400> 154
accacagtcc tgttgggcca gggcttcatg accctttctg tgaaaagcca tattatcacc      60
accccaaatt tttccttaaa tatctttaac tgaaggggtc agcctcttga ctgcaaagac     120
cctaagccgg ttacacagct aactcccact ggccctgatt tgtgaaattg ctgctgcctg     180
attggcacag gagtcgaagg tgttcagctc ccctcctccg tggaacgaga ctctgatttg     240
agtttcacaa attctcgggc cacctcgtca ttgctcctct gaaataaaat ccggagaatg     300
gtcaggcctg tctcatccat atggatcttc cgg                                  333


      <210> 155
      <211> 308
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(308)
      <223> n = A,T,C or G

      <400> 155
actggaaata ataaaaccca catcacagtg ttgtgtcaaa gatcatcagg gcatggatgg      60
gaaagtgctt tgggaactgt aaagtgccta acacatgatc gatgattttt gttataatat     120
ttgaatcacg gtgcatacaa actctcctgc ctgctcctcc tgggccccag ccccagcccc     180
atcacagctc actgctctgt tcatccaggc ccagcatgta gtggctgatt cttcttggct     240
gcttttagcc tccanaagtt tctctgaagc caaccaaacc tctangtgta aggcatgctg     300
gccctggt                                                             308


      <210> 156
      <211> 295
      <212> DNA
```

```
        <213> Homo sapien

        <400> 156
accttgctcg gtgcttggaa catattagga actcaaaata tgagatgata acagtgccta        60
ttattgatta ctgagagaac tgttagacat ttagttgaag attttctaca caggaactga       120
gaataggaga ttatgtttgg ccctcatatt ctctcctatc ctccttgcct cattctatgt       180
ctaatatatt ctcaatcaaa taaggttagc ataatcagga aatcgaccaa ataccaatat       240
aaaaccagat gtctatcctt aagattttca aatagaaaac aaattaacag actat           295

        <210> 157
        <211> 126
        <212> DNA
        <213> Homo sapien

        <400> 157
acaagtttaa atagtgctgt cactgtgcat gtgctgaaat gtgaaatcca ccacatttct        60
gaagagcaaa acaaattctg tcatgtaatc tctatcttgg gtcgtgggta tatctgtccc       120
cttagt                                                                  126

        <210> 158
        <211> 442
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(442)
        <223> n = A,T,C or G

        <400> 158
acccactggt cttggaaaca cccatcctta atacgatgat ttttctgtcg tgtgaaaatg        60
aanccagcag gctgccccta gtcagtcctt ccttccagag aaaaagagat ttgagaaagt       120
gcctgggtaa ttcaccatta atttcctccc ccaaactctc tgagtcttcc cttaatattt       180
ctggtggttc tgaccaaagc aggtcatggt ttgttgagca tttgggatcc cagtgaagta    ·  240
natgtttgta gccttgcata cttagccctt cccacgcaca aacggagtgg cagagtggtg       300
ccaaccctgt tttcccagtc cacgtagaca gattcacagt gcggaattct ggaagctgga       360
nacagacggg ctctttgcag agccgggact ctgagangga catgagggcc tctgcctctg       420
tgttcattct ctgatgtcct gt                                                442

        <210> 159
        <211> 498
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(498)
        <223> n = A,T,C or G

        <400> 159
acttccaggt aacgttgttg tttccgttga gcctgaactg atgggtgacg ttgtaggttc        60
tccaacaaga actgaggttg cagagcgggt agggaagagt gctgttccag ttgcacctgg       120
gctgctgtgg actgttgttg attcctcact acggcccaag gttgtggaac tggcanaaag       180
gtgtgttgtt gganttgagc tcggcggct gtggtaggtt gtgggctctt caacagggc        240
tgctgtggtg ccgggangtg aangtgttgt gtcacttgag cttggccagc tctggaaagt       300
antanattct tcctgaaggc cagcgcttgt ggagctggca ngggtcantg ttgtgtgtaa       360
cgaaccagtg ctgctgtggg tgggtgtana tcctccacaa agcctgaagt tatggtgtcn       420
tcaggtaana atgtggtttc agtgtccctg ggcngctgtg gaaggttgta nattgtcacc       480
```

```
aagggaataa gctgtggt                                                    498
```

```
        <210> 160
        <211> 380
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(380)
        <223> n = A,T,C or G

        <400> 160
acctgcatcc agcttccctg ccaaactcac aaggagacat caacctctag acagggaaac    60
agcttcagga tacttccagg agacagagcc accagcagca aaacaaatat tcccatgcct   120
ggagcatggc atagaggaag ctganaaatg tggggtctga ggaagccatt tgagtctggc   180
cactagacat ctcatcagcc acttgtgtga agagatgccc catgacccca gatgcctctc   240
ccacccttac ctccatctca cacacttgag ctttccactc tgtataattc taacatcctg   300
gagaaaaatg gcagtttgac cgaacctgtt cacaacggta gaggctgatt tctaacgaaa   360
cttgtagaat gaagcctgga                                                380
```

```
        <210> 161
        <211> 114
        <212> DNA
        <213> Homo sapien

        <400> 161
actccacatc ccctctgagc aggcggttgt cgttcaaggt gtatttggcc ttgcctgtca    60
cactgtccac tggcccctta tccacttggt gcttaatccc tcgaaagagc atgt          114
```

```
        <210> 162
        <211> 177
        <212> DNA
        <213> Homo sapien

        <400> 162
actttctgaa tcgaatcaaa tgatacttag tgtagtttta atatcctcat atatatcaaa    60
gttttactac tctgataatt ttgtaaacca ggtaaccaga acatccagtc atacagcttt   120
tggtgatata taacttggca ataacccagt ctggtgatac ataaaactac tcactgt      177
```

```
        <210> 163
        <211> 137
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(137)
        <223> n = A,T,C or G

        <400> 163
catttataca gacaggcgtg aagacattca cgacaaaaac gcgaaattct atcccgtgac    60
canagaaggc agctacggct actcctacat cctggcgtgg gtggccttcg cctgcacctt   120
catcagcggc atgatgt                                                   137
```

```
        <210> 164
        <211> 469
        <212> DNA
```

```
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(469)
        <223> n = A,T,C or G

        <400> 164
cttatcacaa tgaatgttct cctgggcagc gttgtgatct ttgccacctt cgtgacttta      60
tgcaatgcat catgctattt catacctaat gagggagttc caggagattc aaccaggaaa     120
tgcatggatc tcaaaggaaa caaacaccca ataaactcgg agtggcagac tgacaactgt     180
gagacatgca cttgctacga aacagaaatt tcatgttgca cccttgtttc tacacctgtg     240
ggttatgaca aagacaactg ccaaagaatc ttcaagaagg aggactgcaa gtatatcgtg     300
gtggagaaga aggacccaaa aaagacctgt tctgtcagtg aatggataat ctaatgtgct     360
tctagtaggc acagggctcc caggccaggc ctcattctcc tctggcctct aatagtcaat     420
gattgtgtag ccatgcctat cagtaaaaag atntttgagc aaacacttt              469


        <210> 165
        <211> 195
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(195)
        <223> n = A,T,C or G

        <400> 165
acagtttttt atanatatcg acattgccgg cacttgtgtt cagtttcata aagctggtgg      60
atccgctgtc atccactatt ccttggctag agtaaaaatt attcttatag cccatgtccc     120
tgcaggccgc ccgcccgtag ttctcgttcc agtcgtcttg gcacacaggg tgccaggact     180
tcctctgaga tgagt                                                      195


        <210> 166
        <211> 383
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(383)
        <223> n = A,T,C or G

        <400> 166
acatcttagt agtgtggcac atcagggggc catcagggtc acagtcactc atagcctcgc      60
cgaggtcgga gtccacacca ccggtgtagg tgtgctcaat cttgggcttg gcgcccacct     120
ttggagaagg gatatgctgc acacacatgt ccacaaagcc tgtgaactcg ccaaagaatt     180
tttgcagacc agcctgagca aggggcggat gttcagcttc agctcctcct tcgtcaggtg     240
gatgccaacc tcgtctangg tccgtgggaa gctggtgtcc acntcaccta caacctgggc     300
gangatctta taaagaggct ccnagataaa ctccacgaaa cttctctggg agctgctagt     360
nggggccttt ttggtgaact ttc                                            383


        <210> 167
        <211> 247
        <212> DNA
        <213> Homo sapien

        <220>
```

```
        <221> misc_feature
        <222> (1)...(247)
        <223> n = A,T,C or G

        <400> 167
acagagccag accttggcca taaatgaanc agagattaag actaaacccc aagtcganat         60
tggagcagaa actggagcaa gaagtgggcc tggggctgaa gtagagacca aggccactgc        120
tatanccata cacagagcca actctcaggc caaggcnatg gttggggcag anccagagac        180
tcaatctgan tccaaagtgg tggctggaac actggtcatg acanaggcag tgactctgac        240
tgangtc                                                                  247


        <210> 168
        <211> 273
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(273)
        <223> n = A,T,C or G

        <400> 168
acttctaagt tttctagaag tggaaggatt gtantcatcc tgaaaatggg tttacttcaa         60
aatccctcan ccttgttctt cacnactgtc tatactgana gtgtcatgtt tccacaaagg        120
gctgacacct gagcctgnat tttcactcat ccctgagaag ccctttccag tagggtgggc        180
aattcccaac ttccttgcca caagcttccc aggctttctc ccctggaaaa ctccagcttg        240
agtcccagat acactcatgg gctgccctgg gca                                     273


        <210> 169
        <211> 431
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(431)
        <223> n = A,T,C or G

        <400> 169
acagccttgg cttccccaaa ctccacagtc tcagtgcaga aagatcatct tccagcagtc         60
agctcagacc agggtcaaag gatgtgacat caacagtttc tggtttcaga acaggttcta        120
ctactgtcaa atgaccccccc atacttcctc aaaggctgtg gtaagttttg cacaggtgag        180
ggcagcagaa aggggggtant tactgatgga caccatcttc tctgtatact ccacactgac        240
cttgccatgg gcaaaggccc ctaccacaaa aacaatagga tcactgctgg gcaccagctc        300
acgcacatca ctgacaaccg ggatggaaaa agaantgcca actttcatac atccaactgg        360
aaagtgatct gatactggat tcttaattac cttcaaaagc ttctgggggc catcagctgc        420
tcgaacactg a                                                             431


        <210> 170
        <211> 266
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(266)
        <223> n = A,T,C or G
```

```
<400> 170
acctgtgggc tgggctgtta tgcctgtgcc ggctgctgaa agggagttca gaggtggagc    60
tcaaggagct ctgcaggcat tttgccaanc ctctccanag canagggagc aacctacact   120
ccccgctaga aagacaccag attggagtcc tgggaggggg agttggggtg ggcatttgat   180
gtatacttgt cacctgaatg aangagccag agaggaanga gacgaanatg anattggcct   240
tcaaagctag gggtctggca ggtgga                                        266
```

```
<210> 171
<211> 1248
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1248)
<223> n = A,T,C or G
```

```
<400> 171
ggcagccaaa tcataaacgg cgaggactgc agcccgcact cgcagccctg gcaggcggca    60
ctggtcatgg aaaacgaatt gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg   120
tcagccgcac actgtttcca gaagtgagtg cagagctcct acaccatcgg gctgggcctg   180
cacagtcttg aggccgacca agagccaggg agccagatgg tggaggccag cctctccgta   240
cggcacccag agtacaacag acccttgctc gctaacgacc tcatgctcat caagttggac   300
gaatccgtgt ccgagtctga caccatccgg agcatcagca ttgcttcgca gtgccctacc   360
gcggggaact cttgcctcgt ttctggctgg ggtctgctgg cgaacggcag aatgcctacc   420
gtgctgcagt gcgtgaacgt gtcggtggtg tctgaggagg tctgcagtaa gctctatgac   480
ccgctgtacc accccagcat gttctgcgcc ggcggagggc aagaccagaa ggactcctgc   540
aacggtgact ctgggggggcc cctgatctgc aacgggtact gcagggcct tgtgtctttc   600
ggaaaagccc cgtgtggcca agttggcgtg ccaggtgtct acaccaacct ctgcaaattc   660
actgagtgga tagagaaaac cgtccaggcc agttaactct ggggactggg aacccatgaa   720
attgacccco aaatacatcc tgcggaagga attcaggaat atctgttccc agcccctcct   780
ccctcaggcc caggagtcca ggcccccagc ccctcctccc tcaaaccaag ggtacagatc   840
cccagcccct cctccctcag acccaggagt ccagaccccc cagccctcc tccctcagac   900
ccaggagtcc agcccctcct ccctcagacc caggagtcca gacccccag ccctcctcc   960
ctcagaccca ggggtccagg cccccaaccc ctcctccctc agactcagag gtccaagccc  1020
ccaacccntc attccccaga cccagaggtc caggtcccag ccctcntcc ctcagaccca  1080
gcggtccaat gccacctaga ctntccctgt acacagtgcc cccttgtggc acgttgaccc  1140
aaccttacca gttggttttt cattttnngt ccctttcccc tagatccaga ataaagttt   1200
aagagaagng caaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaa              1248
```

```
<210> 172
<211> 159
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(159)
<223> Xaa = Any Amino Acid
```

```
<400> 172
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro
1               5                   10                  15
Leu Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser
            20                  25                  30
Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr
        35                  40                  45
Ala Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly
```

```
        50                    55                    60
Arg Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu
65                    70                    75                    80
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe
                85                    90                    95
Cys Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser
            100                   105                   110
Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe
        115                   120                   125
Gly Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn
    130                   135                   140
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
145                   150                   155
```

        <210> 173
        <211> 1265
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(1265)
        <223> n = A,T,C or G

        <400> 173
```
ggcagcccgc actcgcagcc ctggcaggcg gcactggtca tggaaaacga attgttctgc    60
tcgggcgtcc tggtgcatcc gcagtgggtg ctgtcagccg cacactgttt ccagaactcc   120
tacaccatcg ggctgggcct gcacagtctt gaggccgacc aagagccagg gagccagatg   180
gtggaggcca gcctctccgt acggcaccca gagtacaaca gacccttgct cgctaacgac   240
ctcatgctca tcaagttgga cgaatccgtg tccgagtctg acaccatccg gagcatcagc   300
attgcttcgc agtgccctac cgcggggaac tcttgcctcg tttctggctg gggtctgctg   360
gcgaacggtg agctcacggg tgtgtgtctg ccctcttcaa ggaggtcctc tgcccagtcg   420
cgggggctga cccagagctc tgcgtcccag gcagaatgcc taccgtgctg cagtgcgtga   480
acgtgtcggt ggtgtctgag gaggtctgca gtaagctcta tgacccgctg taccacccca   540
gcatgttctg cgccggcgga gggcaagacc agaaggactc ctgcaacggt gactctgggg   600
ggcccctgat ctgcaacggg tacttgcagg gccttgtgtc tttcggaaaa gccccgtgtg   660
gccaagttgg cgtgccaggt gtctacacca acctctgcaa attcactgag tggatagaga   720
aaaccgtcca ggccagttaa ctctggggac tgggaaccca tgaaattgac ccccaaatac   780
atcctgcgga aggaattcag gaatatctgt tcccagcccc tcctccctca ggcccaggag   840
tccaggcccc cagcccctcc tccctcaaac caagggtaca gatccccagc ccctcctccc   900
tcagacccag gagtccagac ccccccagccc ctcctccctc agacccagga gtccagcccc    960
tcctccntca gacccaggag tccagacccc ccagcccctc ctccctcaga cccagggggtt  1020
gaggcccccca acccctcctc cttcagagtc agaggtccaa gcccccaacc cctcgttccc   1080
cagacccaga ggtnnaggtc ccagcccctc ttccntcaga cccagnggtc caatgccacc  1140
tagatttttcc ctgnacacag tgccccccttg tggnangttg acccaacctt accagttggt  1200
ttttcatttt tngtccctt ccctagatc cagaaataaa gtttaagaga ngngcaaaaa  1260
aaaaa                                                              1265
```

        <210> 174
        <211> 1459
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(1459)
        <223> n = A,T,C or G

```
<400> 174
ggtcagccgc acactgtttc cagaagtgag tgcagagctc ctacaccatc gggctgggcc    60
tgcacagtct tgaggccgac caagagccag ggagccagat ggtggaggcc agcctctccg   120
tacggcaccc agagtacaac agaccettgc tcgctaacga cctcatgctc atcaagttgg   180
acgaatccgt gtccgagtct gacaccatcc ggagcatcag cattgcttcg cagtgcccta   240
ccgcggggaa ctcttgcctc gtttctggct ggggtctgct ggcgaacggt gagctcacgg   300
gtgtgtgtct gccctcttca aggaggtcct ctgcccagtc gcgggggctg acccagagct   360
ctgcgtccca ggcagaatgc ctaccgtgct gcagtgcgtg aacgtgtcgg tggtgtctga   420
ngaggtctgc antaagctct atgacccgct gtaccacccc ancatgttct gcgccggcgg   480
agggcaagac cagaaggact cctgcaacgt gagagagggg aaaggggagg gcaggcgact   540
caggaagggg tggagaaggg ggagacagag acacacaggg ccgcatggcg agatgcagag   600
atggagagac acacaggag acagtgacaa ctagagagag aaactgagag aaacagagaa   660
ataaacacag gaataaagag aagcaaagga agagagaaac agaaacagac atggggaggc   720
agaaacacac acacatagaa atgcagttga ccttccaaca gcatggggcc tgagggcggt   780
gacctccacc caatagaaaa tcctcttata acttttgact ccccaaaaac ctgactagaa   840
atagcctact gttgacgggg agccttacca ataacataaa tagtcgattt atgcatacgt   900
tttatgcatt catgatatac ctttgttgga attttttgat atttctaagc tacacagttc   960
gtctgtgaat ttttttaaat tgttgcaact ctcctaaaat ttttctgatg tgtttattga  1020
aaaaatccaa gtataagtgg acttgtgcat tcaaaccagg gttgttcaag ggtcaactgt  1080
gtacccagag ggaaacagtg acacagattc atagaggtga aacacgaaga gaaacaggaa  1140
aaatcaagac tctacaaaga ggctgggcag ggtggctcat gcctgtaatc ccagcacttt  1200
gggaggcgag gcaggcagat cacttgaggt aaggagttca agaccagcct ggccaaaatg  1260
gtgaaatcct gtctgtacta aaaatacaaa agttagctgg atatggtggc aggcgcctgt  1320
aatcccagct acttgggagg ctgaggcagg agaattgctt gaatatggga ggcagaggtt  1380
gaagtgagtt gagatcacac cactatactc cagctggggc aacagagtaa gactctgtct  1440
caaaaaaaaa aaaaaaaaa                                                1459
```

```
<210> 175
<211> 1167
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(1167)
<223> n = A,T,C or G
```

```
<400> 175
gcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg    60
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg   120
ctgggcctgc acagtcttga ggccgaccaa gagccaggga gccagatggt ggaggccagc   180
ctctccgtac ggcacccaga gtacaacaga ctcttgctcg ctaacgacct catgctcatc   240
aagttggacg aatccgtgtc cgagtctgac accatcggag catcagcat tgcttcgcag   300
tgccctaccg cggggaactc ttgcctcgtn tctggctggg gtctgctggc gaacggcaga   360
atgcctaccg tgctgcactg cgtgaacgtg tcggtggtgt ctgaggangt ctgcagtaag   420
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag   480
gactcctgca acggtgactc tgggggggccc ctgatctgca cgggtactt gcagggcctt   540
gtgtctttcg aaaagcccc gtgtggccaa cttggcgtgc caggtgtcta caccaacctc   600
tgcaaattca ctgagtggat agagaaaacc gtccagncca gttaactctg gggactggga   660
acccatgaaa ttgaccccca aatacatcct gcggaangaa ttcaggaata tctgttccca   720
gcccctcctc cctcaggccc aggagtccag gcccccagcc cctcctccct caaaccaagg   780
gtacagatcc ccagcccctc ctccctcaga cccaggagtc cagacccccc agcccctcnt   840
ccntcagacc caggagtcca gcccctcctc cntcagacgc aggagtccag accccccagc   900
ccntcntccg tcagacccag gggtgcaggc ccccaacccc tcntccntca gagtcagagg   960
tccaagcccc caaccctcg ttccccagac ccagaggtnc aggtcccagc ccctcctccc  1020
tcagacccag cggtccaatg ccacctagan tntccctgta cacagtgccc ccttgtggca  1080
ngttgaccca accttaccag ttggttttc atttttgtc cctttcccct agatccagaa  1140
ataaagtnta agagaagcgc aaaaaaa                                       1167
```

```
<210> 176
<211> 205
<212> PRT
<213> Homo sapien

<220>
<221> VARIANT
<222> (1)...(205)
<223> Xaa = Any Amino Acid

<400> 176
```

Met	Glu	Asn	Glu	Leu	Phe	Cys	Ser	Gly	Val	Leu	Val	His	Pro	Gln	Trp
1				5					10					15	
Val	Leu	Ser	Ala	Ala	His	Cys	Phe	Gln	Asn	Ser	Tyr	Thr	Ile	Gly	Leu
		20					25					30			
Gly	Leu	His	Ser	Leu	Glu	Ala	Asp	Gln	Glu	Pro	Gly	Ser	Gln	Met	Val
		35				40					45				
Glu	Ala	Ser	Leu	Ser	Val	Arg	His	Pro	Glu	Tyr	Asn	Arg	Leu	Leu	Leu
	50				55					60					
Ala	Asn	Asp	Leu	Met	Leu	Ile	Lys	Leu	Asp	Glu	Ser	Val	Ser	Glu	Ser
65				70					75					80	
Asp	Thr	Ile	Arg	Ser	Ile	Ser	Ile	Ala	Ser	Gln	Cys	Pro	Thr	Ala	Gly
			85					90					95		
Asn	Ser	Cys	Leu	Val	Ser	Gly	Trp	Gly	Leu	Leu	Ala	Asn	Gly	Arg	Met
			100					105					110		
Pro	Thr	Val	Leu	His	Cys	Val	Asn	Val	Ser	Val	Val	Ser	Glu	Xaa	Val
		115					120					125			
Cys	Ser	Lys	Leu	Tyr	Asp	Pro	Leu	Tyr	His	Pro	Ser	Met	Phe	Cys	Ala
130					135					140					
Gly	Gly	Gly	Gln	Asp	Gln	Lys	Asp	Ser	Cys	Asn	Gly	Asp	Ser	Gly	Gly
145					150					155					160
Pro	Leu	Ile	Cys	Asn	Gly	Tyr	Leu	Gln	Gly	Leu	Val	Ser	Phe	Gly	Lys
			165					170					175		
Ala	Pro	Cys	Gly	Gln	Leu	Gly	Val	Pro	Gly	Val	Tyr	Thr	Asn	Leu	Cys
		180					185					190			
Lys	Phe	Thr	Glu	Trp	Ile	Glu	Lys	Thr	Val	Gln	Xaa	Ser			
	195					200					205				

```
<210> 177
<211> 1119
<212> DNA
<213> Homo sapien

<400> 177
gcgcactcgc agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc     60
gtcctggtgc atccgcagtg ggtgctgtca gccgcacact gtttccagaa ctcctacacc    120
atcgggctgg gcctgcacag tcttgaggcc gaccaagagc agggagcca gatggtggag     180
gccagcctct ccgtacggca cccagagtac aacagaccct tgctcgctaa cgacctcatg    240
ctcatcaagt tggacgaatc cgtgtccgag tctgacacca tccggagcat cagcattgct    300
tcgcagtgcc ctaccgcggg gaactcttgc ctcgtttctg gctgggggtct gctggcgaac    360
gatgctgtga ttgccatcca gtcccagact gtgggaggct gggagtgtga aagcttttcc    420
caaccctggc agggttgtac catttcggca acttccagtg caaggacgtc ctgctgcatc    480
ctcactgggt gctcactact gctcactgca tcacccggaa cactgtgatc aactagccag    540
caccatagtt ctccgaagtc agactatcat gattactgtg ttgactgtgc tgtctattgt    600
actaaccatg ccgatgttta ggtgaaatta gcgtcacttg gcctcaacca tcttggtatc    660
cagttatcct cactgaattg agatttcctg cttcagtgtc agccattccc acataatttc    720
tgacctacag aggtgaggga tcatatagct cttcaaggat gctggtactc ccctcacaaa    780
```

```
ttcatttctc ctgttgtagt gaaaggtgcg ccctctggag cctcccaggg tgggtgtgca     840
ggtcacaatg atgaatgtat gatcgtgttc ccattaccca aagcctttaa atccctcatg     900
ctcagtacac cagggcaggt ctagcatttc ttcatttagt gtatgctgtc cattcatgca     960
accacctcag gactcctgga ttctctgcct agttgagctc ctgcatgctg cctccttggg    1020
gaggtgaggg agagggccca tggttcaatg ggatctgtgc .agttgtaaca cattaggtgc    1080
ttaataaaca gaagctgtga tgttaaaaaa aaaaaaaaaa                          1119
```

```
        <210> 178
        <211> 164
        <212> PRT
        <213> Homo sapien

        <220>
        <221> VARIANT
        <222> (1)...(164)
        <223> Xaa = Any Amino Acid

        <400> 178
Met Gly Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp
1               5                   10                  15
Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu
            20                  25                  30
Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val
        35                  40                  45
Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu
    50                  55                  60
Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser
65                  70                  75                  80
Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly
            85                  90                  95
Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Asp Ala Val
            100                 105                 110
Ile Ala Ile Gln Ser Xaa Thr Val Gly Gly Trp Glu Cys Glu Lys Leu
        115                 120                 125
Ser Gln Pro Trp Gln Gly Cys Thr Ile Ser Ala Thr Ser Ser Ala Arg
    130                 135                 140
Thr Ser Cys Cys Ile Leu Thr Gly Cys Ser Leu Leu Leu Thr Ala Ser
145                 150                 155                 160
Pro Gly Thr Leu
```

```
        <210> 179
        <211> 250
        <212> DNA
        <213> Homo sapien

        <400> 179
ctggagtgcc ttggtgtttc aagcccctgc aggaagcaga atgcaccttc tgaggcacct      60
ccagctgccc ccggccgggg gatgcgaggc tcggagcacc cttgcccggc tgtgattgct     120
gccaggcact gttcatctca gctttctgt cccttgctc ccggcaagcg cttctgctga     180
aagttcatat ctggagcctg atgtcttaac gaataaaggt cccatgctcc acccgaaaaa     240
aaaaaaaaaa                                                          250
```

```
        <210> 180
        <211> 202
        <212> DNA
        <213> Homo sapien
```

```
        <400> 180
actagtccag tgtggtggaa ttccattgtg ttgggcccaa cacaatggct accttttaaca    60
tcacccagac cccgcccctg cccgtgcccc acgctgctgc taacgacagt atgatgctta   120
ctctgctact cggaaactat ttttatgtaa ttaatgtatg ctttcttgtt tataaatgcc   180
tgatttaaaa aaaaaaaaaa aa                                             202
```

```
        <210> 181
        <211> 558
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(558)
        <223> n = A,T,C or G

        <400> 181
tccytttgkt naggttttkkg agacamccck agacctwaan ctgtgtcaca gacttcyngg    60
aatgtttagg cagtgctagt aatttcytcg taatgattct gttattactt tcctnattct   120
ttattcctct ttcttctgaa gattaatgaa gttgaaaatt gaggtggata aatacaaaaa   180
ggtagtgtga tagtataagt atctaagtgc agatgaaagt gtgttatata tatccattca   240
aaattatgca agttagtaat tactcagggt taactaaatt actttaatat gctgttgaac   300
ctactctgtt ccttggctag aaaaaattat aaacaggact ttgttagttt gggaagccaa   360
attgataata ttctatgttc taaaagttgg gctatacata aattattaag aaatatggaw   420
ttttattccc aggaatatgg kgttcatttt atgaatatta cscrggatag awgtwtgagt   480
aaaaycagtt ttggtwaata ygtwaatatg tcmtaaataa acaakgcttt gacttatttc   540
caaaaaaaa aaaaaaaa                                                  558
```

```
        <210> 182
        <211> 479
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(479)
        <223> n = A,T,C or G

        <400> 182
acagggwttk grggatgcta agsccccrga rwtygtttga tccaaccctg gcttwttttc    60
agaggggaaa atggggccta gaagttacag mscatytagy tggtgcgmtg gcacccctgg   120
cstcacacag astcccgagt agctgggact acaggcacac agtcactgaa gcaggccctg   180
ttwgcaattc acgttgccac ctccaactta aacattcttc atatgtgatg tccttagtca   240
ctaaggttaa actttcccac ccagaaaagg caacttagat aaaatcttag agtactttca   300
tactmttcta agtcctcttc cagcctcact kkgagtcctm cytgggggtt gataggaant   360
ntctcttggc tttctcaata aartctctat ycatctcatg tttaatttgg tacgcatara   420
awtgstgara aaattaaaat gttctggtty macttaaaa araaaaaaaa aaaaaaaa      479
```

```
        <210> 183
        <211> 384
        <212> DNA
        <213> Homo sapien

        <400> 183
aggcgggagc agaagctaaa gccaaagccc aagaagagtg gcagtgccag cactggtgcc    60
agtaccagta ccaataacag tgccagtgcc agtgccagca ccagtggtgg cttcagtgct   120
ggtgccagcc tgaccgccac tctcacattt gggctcttcg ctggccttgg tggagctggt   180
gccagcacca gtggcagctc tggtgcctgt ggtttctcct acaagtgaga ttttagatat   240
```

65

```
tgttaatcct gccagtcttt ctcttcaagc cagggtgcat cctcagaaac ctactcaaca    300
cagcactcta ggcagccact atcaatcaat tgaagttgac actctgcatt aratctattt    360
gccatttcaa aaaaaaaaaa aaaa                                           384
```

```
        <210> 184
        <211> 496
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(496)
        <223> n = A,T,C or G

        <400> 184
accgaattgg gaccgctggc ttataagcga tcatgtyynt ccrgtatkac ctcaacgagc     60
agggagatcg agtctatacg ctgaagaaat ttgacccgat gggacaacag acctgctcag    120
cccatcctgc tcggttctcc ccagatgaca aatactctsg acaccgaatc accatcaaga    180
aacgcttcaa ggtgctcatg acccagcaac cgcgccctgt cctctgaggg tcccttaaac    240
tgatgtcttt tctgccacct gttacccctc ggagactccg taaccaaact cttcggactg    300
tgagccctga tgcctttttg ccagccatac tctttggcat ccagtctctc gtggcgattg    360
attatgcttg tgtgaggcaa tcatggtggc atcacccata aagggaacac atttgacttt    420
tttttctcat attttaaatt actacmagaw tattwmagaw waaatgawtt gaaaaactst    480
taaaaaaaaa aaaaaa                                                    496
```

```
        <210> 185
        <211> 384
        <212> DNA
        <213> Homo sapien

        <400> 185
gctggtagcc tatggcgkgg cccacggagg ggctcctgag gccacggrac agtgacttcc     60
caagtatcyt gcgcsgcgtc ttctaccgtc cctacctgca gatcttcggg cagattcccc    120
aggaggacat ggacgtggcc ctcatggagc acagcaactg ytcgtcggag cccggcttct    180
gggcacaccc tcctggggcc caggcgggca cctgcgtctc ccagtatgcc aactggctgg    240
tggtgctgct cctcgtcatc ttcctgctcg tggccaacat cctgctggtc aacttgctca    300
ttgccatgtt cagttacaca ttcggcaaag tacagggcaa cagcgatctc tactgggaag    360
gcgcagcgtt accgcctcat ccgg                                          384
```

```
        <210> 186
        <211> 577
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(577)
        <223> n = A,T,C or G

        <400> 186
gagttagctc ctccacaacc ttgatgaggt cgtctgcagt ggcctctcgc ttcataccgc     60
tnccatcgtc atactgtagg tttgccacca cytcctggca tcttggggcg gcntaatatt    120
ccaggaaact ctcaatcaag tcaccgtcga tgaaacctgt gggctggttc tgtcttccgc    180
tcggtgtgaa aggatctccc agaaggagtg ctcgatcttc cccacacttt tgatgacttt    240
attgagtcga ttctgcatgt ccagcaggag gttgtaccag ctctctgaca gtgaggtcac    300
cagccctatc atgccgttga mcgtgccgaa garcaccgag ccttgtgtgg gggkkgaagt    360
ctcacccaga ttctgcatta ccagagagcc gtggcaaaag acattgacaa actcgcccag    420
gtggaaaaag amcamctcct ggargtgctn gccgctcctc gtcmgttggt ggcagcgctw    480
```

```
tccttttgac acacaaacaa gttaaaggca ttttcagccc ccagaaantt gtcatcatcc    540
aagatntcgc acagcactna tccagttggg attaaat                            577
```

```
        <210> 187
        <211> 534
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(534)
        <223> n = A,T,C or G

        <400> 187
aacatcttcc tgtataatgc tgtgtaatat cgatccgatn ttgtctgstg agaatycatw    60
actkggaaaa gmaacattaa agcctggaca ctggtattaa aattcacaat atgcaacact   120
ttaaacagtg tgtcaatctg ctcccyynac tttgtcatca ccagtctggg aakaagggta   180
tgccctattc acacctgtta aaagggcgct aagcattttt gattcaacat cttttttttt   240
gacacaagtc cgaaaaaagc aaaagtaaac agttatyaat ttgttagcca attcactttc   300
ttcatgggac agagccatyt gatttaaaaa gcaaattgca taatattgag cttygggagc   360
tgatatttga gcggaagagt agcctttcta cttcaccaga cacaactccc tttcatattg   420
ggatgttnac naaagtwatg tctctwacag atgggatgct tttgtggcaa ttctgttctg   480
aggatctccc agtttattta ccacttgcac aagaaggcgt tttcttcctc aggc         534
```

```
        <210> 188
        <211> 761
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(761)
        <223> n = A,T,C or G

        <400> 188
agaaaccagt atctctnaaa acaacctctc ataccttgtg gacctaattt tgtgtgcgtg    60
tgtgtgtgcg cgcatattat atagacaggc acatcttttt tacttttgta aaagcttatg   120
cctctttggt atctatatct gtgaaagttt taatgatctg ccataatgtc ttggggacct   180
ttgtcttctg tgtaaatggt actagagaaa acacctatnt tatgagtcaa tctagttngt   240
tttattcgac atgaaggaaa tttccagatn acaacactna caaactctcc ctkgackarg   300
ggggacaaag aaaagcaaaa ctgamcataa raaacaatwa cctggtgaga arttgcataa   360
acagaaatwr ggtagtatat tgaarnacag catcattaaa rmgttwtktt wttctccctt   420
gcaaaaaaca tgtacngact tcccgttgag taatgccaag ttgttttttt tatnataaaa   480
cttgcccttc attacatgtt tnaaagtggt gtggtgggcc aaaatattga aatgatggaa   540
ctgactgata aagctgtaca aataagcagt gtgcctaaca agcaacacag taatgttgac   600
atgcttaatt cacaaatgct aatttcatta taaatgtttg ctaaaataca ctttgaacta   660
tttttctgtn ttcccagagc tgagatntta gattttatgt agtatnaagt gaaaaantac   720
gaaataata acattgaaga aaaananaaa aaanaaaaaa a                        761
```

```
        <210> 189
        <211> 482
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(482)
        <223> n = A,T,C or G
```

<400> 189
```
tttttttttt tttgccgatn ctactatttt attgcaggan gtgggggtgt atgcaccgca    60
caccggggct atnagaagca agaaggaagg agggagggca cagccccttg ctgagcaaca   120
aagccgcctg ctgccttctc tgtctgtctc ctggtgcagg cacatgggga gaccttcccc   180
aaggcagggg ccaccagtcc aggggtggga atacagggggg tgggangtgt gcataagaag   240
tgataggcac aggccacccg gtacagaccc ctcggctcct gacaggtnga tttcgaccag   300
gtcattgtgc cctgcccagg cacagcgtan atctggaaaa gacagaatgc tttccttttc   360
aaatttggct ngtcatngaa ngggcanttt tccaanttng gctnggtctt ggtacncttg   420
gttcggccca gctccncgtc caaaaantat tcacccnnct ccnaattgct tgcnggnccc   480
cc                                                                 482
```

<210> 190
<211> 471
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(471)
<223> n = A,T,C or G

<400> 190
```
tttttttttt ttttaaaaca gttttccaca acaaaattta ttagaagaat agtggttttg    60
aaaactctcg catccagtga gaactaccat acaccacatt acagctngga atgtnctcca   120
aatgtctggt caaatgatac aatggaacca ttcaatctta cacatgcacg aaagaacaag   180
cgcttttgac atacaatgca caaaaaaaaa aggggggggg gaccacatgg attaaaattt   240
taagtactca tcacatacat taagacacag ttctagtcca gtcnaaaatc agaactgcnt   300
tgaaaaattt catgtatgca atccaaccaa agaacttnat tggtgatcat gantnctcta   360
ctacatcnac cttgatcatt gccaggaacn aaaagttnaa ancacncngt acaaaaanaa   420
tctgtaattn anttcaacct ccgtacngaa aaatnttnnt tatacactcc c            471
```

<210> 191
<211> 402
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(402)
<223> n = A,T,C or G

<400> 191
```
gagggattga aggtctgttc tastgtcggm ctgttcagcc accaactcta acaagttgct    60
gtcttccact cactgtctgt aagcttttta acccagacwg tatcttcata aatagaacaa   120
attcttcacc agtcacatct tctaggacct ttttggattc agttagtata agctcttcca   180
cttcctttgt taagacttca tctggtaaag tcttaagttt tgtagaaagg aattyaattg   240
ctcgttctct aacaatgtcc tctccttgaa gtatttggct gaacaaccca cctaaagtcc   300
ctttgtgcat ccattttaaa tatacttaat agggcattgk tncactaggt taaattctgc   360
aagagtcatc tgtctgcaaa agttgcgtta gtatatctgc ca                      402
```

<210> 192
<211> 601
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature

```
        <222> (1)...(601)
        <223> n = A,T,C or G

        <400> 192
gagctcggat ccaataatct ttgtctgagg gcagcacaca tatncagtgc catggnaact    60
ggtctacccc acatgggagc agcatgccgt agntatataa ggtcattccc tgagtcagac   120
atgcytyttt gaytaccgtg tgccaagtgc tggtgattct yaacacacyt ccatcccgyt   180
cttttgtgga aaaactggca cttktctgga actagcarga catcacttac aaattcaccc   240
acgagacact tgaaaggtgt aacaaagcga ytcttgcatt gctttttgtc cctccggcac   300
cagttgtcaa tactaacccg ctggtttgcc tccatcacat ttgtgatctg tagctctgga   360
tacatctcct gacagtactg aagaacttct tcttttgttt caaaagcarc tcttggtgcc   420
tgttggatca ggttcccatt tcccagtcyg aatgttcaca tggcatattt wacttcccac   480
aaaacattgc gatttgaggc tcagcaacag caaatcctgt tccggcattg gctgcaagag   540
cctcgatgta gccggccagc gccaaggcag gcgccgtgag ccccaccagc agcagaagca   600
g                                                                   601

        <210> 193
        <211> 608
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(608)
        <223> n = A,T,C or G

        <400> 193
atacagccca natcccacca cgaagatgcg cttgttgact gagaacctga tgcggtcact    60
ggtcccgctg tagccccagc gactctccac ctgctggaag cggttgatgc tgcactcytt   120
cccaacgcag gcagmagcgg gsccggtcaa tgaactccay tcgtggcttg gggtkgacgg   180
tkaagtgcag gaagaggctg accacctcgc ggtccaccag gatgcccgac tgtgcgggac   240
ctgcagcgaa actcctcgat ggtcatgagc gggaagcgaa tgaggcccag ggccttgccc   300
agaaccttcc gcctgttctc tggcgtcacc tgcagctgct gccgctgaca ctcggcctcg   360
gaccagcgga caaacggcrt tgaacagccg cacctcacgg atgcccagtg tgtcgcgctc   420
caggammgsc accagcgtgt ccaggtcaat gtcggtgaag ccctccgcgg gtratggcgt   480
ctgcagtgtt tttgtcgatg ttctccaggc acaggctggc cagctgcggt tcatcgaaga   540
gtcgcgcctg cgtgagcagc atgaaggcgt tgtcggctcg cagttcttct tcaggaactc   600
cacgcaat                                                            608

        <210> 194
        <211> 392
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(392)
        <223> n = A,T,C or G

        <400> 194
gaacggctgg accttgcctc gcattgtgct tgctggcagg gaataccttg gcaagcagyt    60
ccagtccgag cagccccaga ccgctgccgc ccgaagctaa gcctgcctct ggccttcccc   120
tccgcctcaa tgcagaacca gtagtgggag cactgtgttt agagttaaga gtgaacactg   180
tttgatttta cttgggaatt tcctctgtta tatagctttt cccaatgcta atttccaaac   240
aacaacaaca aaataacatg tttgcctgtt aagttgtata aaagtaggtg attctgtatt   300
taaagaaaat attactgtta catatactgc ttgcaatttc tgtatttatt gktnctstgg   360
aaataaatat agttattaaa ggttgtcant cc                                 392
```

```
<210> 195
<211> 502
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(502)
<223> n = A,T,C or G

<400> 195
ccsttkgagg ggtkaggkyc cagttyccga gtggaagaaa caggccagga gaagtgcgtg      60
ccgagctgag gcagatgttc ccacagtgac ccccagagcc stgggstata gtytctgacc     120
cctcncaagg aaagaccacs ttctggggac atgggctgga gggcaggacc tagaggcacc     180
aagggaaggc cccattccgg ggstgttccc cgaggaggaa gggaaggggc tctgtgtgcc     240
ccccasgagg aagaggccct gagtcctggg atcagacacc ccttcacgtg tatccccaca     300
caaatgcaag ctcaccaagg tccctctca gtccccttcc stacaccctg amcggccact      360
gscscacacc cacccagagc acgccacccg ccatggggar tgtgctcaag gartcgcngg     420
gcarcgtgga catctngtcc cagaaggggg cagaatctcc aatagangga ctgarcmstt     480
gctnanaaaa aaaaanaaaa aa                                              502
```

```
<210> 196
<211> 665
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(665)
<223> n = A,T,C or G

<400> 196
ggttacttgg tttcattgcc accacttagt ggatgtcatt tagaaccatt ttgtctgctc      60
cctctggaag ccttgcgcag agcggacttt gtaattgttg gagaataact gctgaatttt     120
wagctgtttk gagttgatts gcaccactgc acccacaact tcaatatgaa aacyawttga     180
actwatttat tatcttgtga aaagtataac aatgaaaatt ttgttcatac tgtattkatc     240
aagtatgatg aaaagcaawa gatatatatt cttttattat gttaaattat gattgccatt     300
attaatcggc aaaatgtgga gtgtatgttc ttttcacagt aatatatgcc ttttgtaact     360
tcacttggtt attttattgt aaatgartta caaaattctt aatttaagar aatggtatgt     420
watatttatt tcattaattt ctttcctkgt ttacgtwaat tttgaaaaga wtgcatgatt     480
tcttgacaga aatcgatctt gatgctgtgg aagtagtttg acccacatcc ctatgagttt     540
ttcttagaat gtataaaggt tgtagcccat cnaacttcaa agaaaaaaat gaccacatac     600
tttgcaatca ggctgaaatg tggcatgctn ttctaattcc aactttataa actagcaaan     660
aagtg                                                                 665
```

```
<210> 197
<211> 492
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(492)
<223> n = A,T,C or G

<400> 197
ttttnttttt tttttttgc aggaaggatt ccatttattg tggatgcatt ttcacaatat      60
atgtttattg gagcgatcca ttatcagtga aaagtatcaa gtgtttataa natttttagg     120
```

```
aaggcagatt cacagaacat gctngtcngc ttgcagtttt acctcgtana gatnacagag          180
aattatagtc naaccagtaa acnaggaatt tactttttcaa aagattaaat ccaaactgaa          240
caaaattcta ccctgaaact tactccatcc aaatattgga ataanagtca gcagtgatac          300
attctcttct gaactttaga ttttctagaa aaatatgtaa tagtgatcag gaagagctct          360
tgttcaaaag tacaacnaag caatgttccc ttaccatagg ccttaattca aactttgatc          420
catttcactc ccatcacggg agtcaatgct acctgggaca cttgtatttt gttcatnctg          480
ancntggctt aa                                                              492
```

        <210> 198
        <211> 478
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(478)
        <223> n = A,T,C or G

        <400> 198
```
tttntttttgn atttcantct gtannaanta ttttcattat gtttattana aaaatatnaa          60
tgtntccacn acaaatcatn ttacntnagt aagaggccan ctacattgta caacatacac          120
tgagtatatt ttgaaaagga caagtttaaa gtanacncat attgccganc atancacatt          180
tatacatggc ttgattgata tttagcacag canaaactga gtgagttacc agaaanaaat          240
natatatgtc aatcngattt aagatacaaa acagatccta tggtacatan catcntgtag          300
gagttgtggc tttatgttta ctgaaagtca atgcagttcc tgtacaaaga gatggccgta          360
agcattctag tacctctact ccatggttaa gaatcgtaca cttatgttta catatgtnca          420
gggtaagaat tgtgttaagt naanttatgg agaggtccan gagaaaaatt tgatncaa           478
```

        <210> 199
        <211> 482
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(482)
        <223> n = A,T,C or G

        <400> 199
```
agtgacttgt cctccaacaa aacccccttga tcaagtttgt ggcactgaca atcagaccta          60
tgctagttcc tgtcatctat tcgctactaa atgcagactg gaggggacca aaaaggggca          120
tcaactccag ctggattatt ttggagcctg caaatctatt cctacttgta cggactttga          180
agtgattcag tttcctctac ggatgagaga ctggctcaag aatatcctca tgcagcttta          240
tgaagccnac tctgaacacg ctggttatct nagatgagaa ncagagaaat aaagtcnaga          300
aaatttacct ggangaaaag aggctttngg ctggggacca tcccattgaa ccttctctta          360
anggacttta agaanaaact accacatgtn tgtngtatcc tggtgccngg ccgtttantg          420
aacntngacn ncacccttnt ggaatanant cttgacngcn tcctgaactt gctcctctgc          480
ga                                                                          482
```

        <210> 200
        <211> 270
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(270)
        <223> n = A,T,C or G

```
        <400> 200
cggccgcaag tgcaactcca gctggggccg tgcggacgaa gattctgcca gcagttggtc      60
cgactgcgac gacggcggcg gcgacagtcg caggtgcagc gcgggcgcct ggggtcttgc     120
aaggctgagc tgacgccgca gaggtcgtgt cacgtcccac gaccttgacg ccgtcgggga     180
cagccggaac agagcccggt gaangcggga ggcctcgggg agccctcgg  gaagggcggc     240
ccgagagata cgcaggtgca ggtggccgcc                                      270

        <210> 201
        <211> 419
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(419)
        <223> n = A,T,C or G

        <400> 201
tttttttttt ttttggaatc tactgcgagc acagcaggtc agcaacaagt ttattttgca      60
gctagcaagg taacagggta gggcatggtt acatgttcag gtcaacttcc tttgtcgtgg     120
ttgattggtt tgtctttatg ggggcggggt ggggtagggg aaancgaagc anaantaaca    180
tggagtgggt gcaccctccc tgtagaacct ggttacnaaa gcttggggca gttcacctgg    240
tctgtgaccg tcattttctt gacatcaatg ttattagaag tcaggatatc ttttagagag    300
tccactgtnt ctggagggag attagggttt cttgccaana tccaancaaa atccacntga    360
aaaagttgga tgatncangt acngaatacc ganggcatan ttctcatant cggtggcca    419

        <210> 202
        <211> 509
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(509)
        <223> n = A,T,C or G

        <400> 202
tttntttttt tttttttttt tttttttttt tttttttttt tttttttttt tttttttttt      60
tggcacttaa tccatttttta tttcaaaatg tctacaaant ttnaatncnc cattatacng     120
gtnattttnc aaaatctaaa nnttattcaa atntnagcca aantccttac ncaaatnnaa     180
tacncncaaa aatcaaaaat atacntntct ttcagcaaac ttngttacat aaaattaaaaa    240
aatatatacg gctggtgttt tcaaagtaca attatcttaa cactgcaaac atntttnnaa     300
ggaactaaaa taaaaaaaaa cactnccgca aaggttaaag ggaacaacaa attcntttta     360
caacancnnc nattataaaa atcatatctc aaatcttagg ggaatatata cttcacacng     420
ggatcttaac ttttactnca ctttgtttat ttttttanaa ccattgtntt gggcccaaca     480
caatggnaat nccnccncnc tggactagt                                      509

        <210> 203
        <211> 583
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(583)
        <223> n = A,T,C or G
```

```
<400> 203
tttttttttt tttttttga cccccctctt ataaaaaaca agttaccatt ttatttact        60
tacacatatt tattttataa ttggtattag atattcaaaa ggcagctttt aaaatcaaac       120
taaatggaaa ctgccttaga tacataattc ttaggaatta gcttaaaatc tgcctaaagt       180
gaaaatcttc tctagctctt ttgactgtaa atttttgact cttgtaaaac atccaaattc       240
attttcttg tctttaaaat tatctaatct ttccatttt tccctattcc aagtcaattt        300
gcttctctag cctcatttcc tagctcttat ctactattag taagtggctt ttttcctaaa      360
agggaaaaca ggaagagana atggcacaca aaacaaacat tttatattca tatttctacc      420
tacgttaata aaatagcatt ttgtgaagcc agctcaaaag aaggcttaga tcctttatg       480
tccattttag tcactaaacg atatcnaaag tgccagaatg caaaaggttt gtgaacattt       540
attcaaaagc taatataaga tatttcacat actcatcttt ctg                        583


        <210> 204
        <211> 589
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(589)
        <223> n = A,T,C or G

        <400> 204
ttttttttnt tttttttttt tttttnctc ttcttttttt ttganaatga ggatcgagtt       60
tttcactctc tagatagggc atgaagaaaa ctcatctttc cagctttaaa ataacaatca      120
aatctcttat gctatatcat attttaagtt aaactaatga gtcactggct tatcttctcc      180
tgaaggaaat ctgttcattc ttctcattca tatagttata tcaagtacta ccttgcatat      240
tgagaggttt ttcttctcta tttacacata tatttccatg tgaatttgta tcaaaccttt      300
attttcatgc aaactagaaa ataatgtntt cttttgcata agagaagaga acaatatnag      360
cattacaaaa ctgctcaaat tgtttgttaa gnttatccat tataattagt tnggcaggag      420
ctaatacaaa tcacatttac ngacnagcaa taataaaact gaagtaccag ttaaatatcc      480
aaaataatta aaggaacatt tttagcctgg gtataattag ctaattcact ttacaagcat      540
ttattnagaa tgaattcaca tgttattatt ccntagccca acacaatgg                  589


        <210> 205
        <211> 545
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(545)
        <223> n = A,T,C or G

        <400> 205
tttttntttt tttttcagt aataatcaga acaatatttta ttttatatt taaaattcat       60
agaaaagtgc cttacattta ataaaagttt gtttctcaaa gtgatcagag gaattagata      120
tngtcttgaa caccaatatt aatttgagga aaatacacca aaatacatta agtaaattat      180
ttaagatcat agagcttgta agtgaaaaga taaaatttga cctcagaaac tctgagcatt      240
aaaaatccac tattagcaaa taaattacta tggacttctt gctttaattt tgtgatgaat      300
atggggtgtc actggtaaac caacacattc tgaaggatac attacttagt gatagattct      360
tatgtacttt gctanatnac gtggatatga gttgacaagt ttctctttct tcaatctttt      420
aaggggcnga ngaaatgagg aagaaaagaa aaggattacg catactgttc tttctatngg      480
aaggattaga tatgtttcct ttgccaatat taaaaaaata ataatgttta ctactagtga      540
aaccc                                                                  545


        <210> 206
        <211> 487
```

```
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(487)
        <223> n = A,T,C or G

        <400> 206
ttttttttttt tttttttagtc aagtttctna ttttttattat aattaaagtc ttggtcattt        60
catttattag ctctgcaact tacatattta aattaaagaa acgttnttag acaactgtna       120
caatttataa atgtaaggtg ccattattga gtanatatat tcctccaaga gtggatgtgt       180
cccttctccc accaactaat gaancagcaa cattagttta atttttattag tagatnatac       240
actgctgcaa acgctaattc tcttctccat ccccatgtng atattgtgta tatgtgtgag       300
ttggtnagaa tgcatcanca atctnacaat caacagcaag atgaagctag gcntgggctt       360
tcggtgaaaa tagactgtgt ctgtctgaat caaatgatct gacctatcct cggtggcaag       420
aactcttcga accgcttcct caaaggcngc tgccacattt gtggcntctn ttgcacttgt       480
ttcaaaa                                                                  487


        <210> 207
        <211> 332
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(332)
        <223> n = A,T,C or G

        <400> 207
tgaattggct aaaagactgc attttttanaa ctagcaactc ttatttctttt cctttaaaaa        60
tacatagcat taaatcccaa atcctattta aagacctgac agcttgagaa ggtcactact       120
gcatttatag gaccttctgg tggttctgct gttacntttg aantctgaca atccttgana       180
atctttgcat gcagaggagg taaaaggtat tggatttttca cagaggaana acacagcgca       240
gaaatgaagg ggccaggctt actgagcttg tccactggag ggctcatggg tgggacatgg       300
aaaagaaggc agcctaggcc ctggggagcc ca                                      332


        <210> 208
        <211> 524
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(524)
        <223> n = A,T,C or G

        <400> 208
agggcgtggt gcggagggcg ttactgtttt gtctcagtaa caataaatac aaaaagactg        60
gttgtgttcc ggccccatcc aaccacgaag ttgatttctc ttgtgtgcag agtgactgat       120
tttaaaggac atggagcttg tcacaatgtc acaatgtcac agtgtgaagg gcacactcac       180
tcccgcgtga ttcacattta gcaaccaaca atagctcatg agtccatact tgtaaatact       240
tttggcagaa tacttnttga aacttgcaga tgataactaa gatccaagat atttcccaaa       300
gtaaatagaa gtgggtcata atattaatta cctgttcaca tcagcttcca tttacaagtc       360
atgagcccag acactgacat caaactaagc ccacttagac tcctcaccac cagtctgtcc       420
tgtcatcaga caggaggctg tcaccttgac caaattctca ccagtcaatc atctatccaa       480
aaaccattac ctgatccact tccggtaatg caccaccttg gtga                        524
```

```
        <210> 209
        <211> 159
        <212> DNA
        <213> Homo sapien

        <400> 209
gggtgaggaa atccagagtt gccatggaga aaattccagt gtcagcattc ttgctccttg        60
tggccctctc ctacactctg gccagagata ccacagtcaa acctggagcc aaaaaggaca       120
caaaggactc tcgacccaaa ctgccccaga ccctctcca                               159


        <210> 210
        <211> 256
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(256)
        <223> n = A,T,C or G

        <400> 210
actccctggc agacaaaggc agaggagaga gctctgttag ttctgtgttg ttgaactgcc        60
actgaatttc tttccacttg gactattaca tgccanttga gggactaatg gaaaaacgta       120
tggggagatt ttanccaatt tangtntgta aatggggaga ctggggcagg cgggagagat       180
ttgcagggtg naaatgggan ggctggtttg ttanatgaac agggacatag gaggtaggca       240
ccaggatgct aaaatca                                                       256


        <210> 211
        <211> 264
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(264)
        <223> n = A,T,C or G

        <400> 211
acattgtttt tttgagataa agcattgaga gagctctcct taacgtgaca caatggaagg        60
actggaacac atacccacat ctttgttctg agggataatt ttctgataaa gtcttgctgt       120
atattcaagc acatatgtta tatattattc agttccatgt ttatagccta gttaaggaga       180
ggggagatac attcngaaag aggactgaaa gaaatactca agtnggaaaa cagaaaaaga       240
aaaaaaggag caaatgagaa gcct                                               264


        <210> 212
        <211> 328
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(328)
        <223> n = A,T,C or G

        <400> 212
acccaaaaat ccaatgctga atatttggct tcattattcc canattcttt gattgtcaaa        60
ggatttaatg ttgtctcagc ttgggcactt cagttaggac ctaaggatgc cagccggcag       120
gtttatatat gcagcaacaa tattcaagcg cgacaacagg ttattgaact tgcccgccag       180
```

```
ttnaatttca ttcccattga cttgggatcc ttatcatcag ccagagagat tgaaaattta          240
cccctacnac tctttactct ctgganaggg ccagtggtgg tagctataag cttggccaca          300
ttttttttc ctttattcct ttgtcaga                                              328
```

```
        <210> 213
        <211> 250
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(250)
        <223> n = A,T,C or G

        <400> 213
acttatgagc agagcgacat atccnagtgt agactgaata aaactgaatt ctctccagtt          60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct          120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt          180
ttcaatattt gcatgaacct gctgataanc catgttaana aacaaatatc tctctnacct          240
tctcatcggt                                                                 250
```

```
        <210> 214
        <211> 444
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(444)
        <223> n = A,T,C or G

        <400> 214
acccagaatc caatgctgaa tatttggctt cattattccc agattctttg attgtcaaag          60
gatttaatgt tgtctcagct tgggcacttc agttaggacc taaggatgcc agccggcagg          120
tttatatatg cagcaacaat attcaagcgc gacaacaggt tattgaactt gcccgccagt          180
tgaatttcat tcccattgac ttgggatcct tatcatcagc canagagatt gaaaatttac          240
ccctacgact ctttactctc tggagagggc cagtggtggt agctataagc ttggccacat          300
ttttttttc tttattcctt tgtcagagat gcgattcatc catatgctan aaaccaacag          360
agtgactttt acaaaattcc tataganatt gtgaataaaa ccttacctat agttgccatt          420
actttgctct ccctaatata cctc                                                444
```

```
        <210> 215
        <211> 366
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(366)
        <223> n = A,T,C or G

        <400> 215
acttatgagc agagcgacat atccaagtgt anactgaata aaactgaatt ctctccagtt          60
taaagcattg ctcactgaag ggatagaagt gactgccagg agggaaagta agccaaggct          120
cattatgcca aagganatat acatttcaat tctccaaact tcttcctcat tccaagagtt          180
ttcaatattt gcatgaacct gctgataagc catgttgaga aacaaatatc tctctgacct          240
tctcatcggt aagcagaggc tgtaggcaac atggaccata gcgaanaaaa aacttagtaa          300
tccaagctgt tttctacact gtaaccaggt ttccaaccaa ggtggaaatc tcctatactt          360
```

```
ggtgcc                                                                    366
```

```
        <210> 216
        <211> 260
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(260)
        <223> n = A,T,C or G

        <400> 216
ctgtataaac agaactccac tgcangaggg agggccgggc caggagaatc tccgcttgtc       60
caagacaggg gcctaaggag ggtctccaca ctgctnntaa gggctnttnc attttttat       120
taataaaaag tnnaaaaggc ctcttctcaa ctttttttccc ttnggctgga aaatttaaaa     180
atcaaaaatt tcctnaagtt ntcaagctat catatatact ntatcctgaa aaagcaacat      240
aattcttcct tccctccttt                                                  260

        <210> 217
        <211> 262
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(262)
        <223> n = A,T,C or G

        <400> 217
acctacgtgg gtaagtttan aaatgttata atttcaggaa naggaacgca tataattgta      60
tcttgcctat aattttctat tttaataagg aaatagcaaa ttggggtggg gggaatgtag      120
ggcattctac agtttgagca aaatgcaatt aaatgtggaa ggacagcact gaaaaatttt      180
atgaataatc tgtatgatta tatgtctcta gagtagattt ataattagcc acttacccta     240
atatccttca tgcttgtaaa gt                                               262

        <210> 218
        <211> 205
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(205)
        <223> n = A,T,C or G

        <400> 218
accaaggtgg tgcattaccg gaantggatc aangacacca tcgtggccaa cccctgagca      60
cccctatcaa ctcccttttg tagtaaactt ggaaccttgg aaatgaccag gccaagactc      120
aggcctcccc agttctactg acctttgtcc ttangtntna ngtccagggt tgctaggaaa      180
anaaatcagc agacacaggt gtaaa                                            205

        <210> 219
        <211> 114
        <212> DNA
        <213> Homo sapien

        <400> 219
```

```
tactgttttg tctcagtaac aataaataca aaaagactgg ttgtgttccg gccccatcca        60
accacgaagt tgatttctct tgtgtgcaga gtgactgatt ttaaaggaca tgga            114
```

```
<210> 220
<211> 93
<212> DNA
<213> Homo sapien
```

```
<400> 220
actagccagc acaaaaggca gggtagcctg aattgctttc tgctctttac atttctttta        60
aaataagcat ttagtgctca gtccctactg agt                                    93
```

```
<210> 221
<211> 167
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(167)
<223> n = A,T,C or G
```

```
<400> 221
actangtgca ggtgcgcaca aatatttgtc gatattccct tcatcttgga ttccatgagg        60
tcttttgccc agcctgtggc tctactgtag taagtttctg ctgatgagga gccagnatgc       120
cccccactac cttccctgac gctccccana aatcacccaa cctctgt                     167
```

```
<210> 222
<211> 351
<212> DNA
<213> Homo sapien
```

```
<400> 222
agggcgtggt gcggagggcg gtactgacct cattagtagg aggatgcatt ctggcacccc        60
gttcttcacc tgtcccccaa tccttaaaag gccatactgc ataaagtcaa caacagataa       120
atgtttgctg aattaaagga tggatgaaaa aaattaataa tgaatttttg cataatccaa       180
ttttctcttt tatatttcta gaagaagttt ctttgagcct attagatccc gggaatcttt       240
taggtgagca tgattagaga gcttgtaggt tgcttttaca tatatctggc atatttgagt       300
ctcgtatcaa aacaatagat tggtaaaggt ggtattattg tattgataag t               351
```

```
<210> 223
<211> 383
<212> DNA
<213> Homo sapien
```

```
<220>
<221> misc_feature
<222> (1)...(383)
<223> n = A,T,C or G
```

```
<400> 223
aaaacaaaca aacaaaaaaa acaattcttc attcagaaaa attatcttag ggactgatat        60
tggtaattat ggtcaattta atwrtrttkt ggggcatttc cttacattgt cttgacaaga       120
ttaaaatgtc tgtgccaaaa ttttgtattt tatttggaga cttcttatca aaagtaatgc       180
tgccaaagga agtctaagga attagtagtg ttcccmtcac ttgtttggag tgtgctattc       240
taaaagattt tgatttcctg gaatgacaat tatattttaa ctttggtggg ggaaanagtt       300
ataggaccac agtcttcact tctgatactt gtaaattaat cttttattgc acttgttttg       360
accattaagc tatatgttta aaa                                               383
```

```
<210> 224
<211> 320
<212> DNA
<213> Homo sapien

<400> 224
cccctgaagg cttcttgtta gaaaatagta cagttacaac caataggaac aacaaaaaga        60
aaaagtttgt gacattgtag tagggagtgt gtaccccttat ctccccatca aaaaaaaaat       120
ggatacatgg ttaaaggata raagggcaat attttatcat atgttctaaa agagaaggaa       180
gagaaaatac tactttctcr aaatggaagc ccttaaaggt gctttgatac tgaaggacac       240
aaatgtggcc gtccatcctc ctttaragtt gcatgacttg gacacggtaa ctgttgcagt       300
tttaractcm gcattgtgac                                                    320


<210> 225
<211> 1214
<212> DNA
<213> Homo sapien

<400> 225
gaggactgca gcccgcactc gcagccctgg caggcggcac tggtcatgga aaacgaattg        60
ttctgctcgg gcgtcctggt gcatccgcag tgggtgctgt cagccgcaca ctgtttccag       120
aactcctaca ccatcgggct gggcctgcac agtcttgagg ccgaccaaga gccagggagc       180
cagatggtgg aggccagcct ctccgtacgg cacccagagt acaacagacc cttgctcgct       240
aacgacctca tgctcatcaa gttggacgaa tccgtgtccg agtctgacac catccggagc       300
atcagcattg cttcgcagtg ccctaccgcg gggaactctt gcctcgtttc tggctggggt       360
ctgctggcga acggcagaat gcctaccgtg ctgcagtgcg tgaacgtgtc ggtggtgtct       420
gaggaggtct gcagtaagct ctatgacccg ctgtaccacc ccagcatgtt ctgcgccggc       480
ggagggcaag accagaagga ctcctgcaac ggtgactctg ggggcccct gatctgcaac        540
gggtacttgc agggccttgt gtctttcgga aaagccccgt gtggccaagt ggcgtgcca        600
ggtgtctaca ccaacctctg caaattcact gagtggatag agaaaaccgt ccaggccagt       660
taactctggg gactgggaac ccatgaaatt gaccccaaa tacatcctgc ggaaggaatt        720
caggaatatc tgttcccagc ccctcctccc tcaggcccag gagtccaggc ccccagcccc       780
tcctccctca aaccaagggt acagatcccc agccctcct ccctcagacc caggagtcca        840
gaccccccag cccctcctcc ctcagaccca ggagtccagc ccctcctccc tcagacccag       900
gagtccagac cccccagccc ctcctccctc agacccaggg tccaggccc ccaacccctc        960
ctccctcaga ctcagaggtc caagccccca ccctccctt ccccagaccc agaggtccag       1020
gtcccagccc ctcctccctc agacccagcg gtccaatgcc acctagactc tccctgtaca      1080
cagtgcccc ttgtggcacg ttgacccaac cttaccagtt ggttttttcat tttttgtccc      1140
tttccctag atccagaaat aaagtctaag agaagcgcaa aaaaaaaaa aaaaaaaaa       1200
aaaaaaaaaa aaaa                                                        1214


<210> 226
<211> 119
<212> DNA
<213> Homo sapien

<400> 226
acccagtatg tgcagggaga cggaacccca tgtgacagcc cactccacca gggttcccaa        60
agaacctggc ccagtcataa tcattcatcc tgacagtggc aataatcacg ataaccagt       119


<210> 227
<211> 818
<212> DNA
<213> Homo sapien

<400> 227
acaattcata gggacgacca atgaggacag ggaatgaacc cggctctccc ccagccctga        60
```

```
tttttgctac atatggggtc ccttttcatt ctttgcaaaa acactgggtt ttctgagaac      120
acggacggtt cttagcacaa tttgtgaaat ctgtgtaraa ccgggctttg caggggagat      180
aattttcctc ctctggagga aaggtggtga ttgacaggca gggagacagt gacaaggcta      240
gagaaagcca cgctcggcct tctctgaacc aggatggaac ggcagacccc tgaaaacgaa      300
gcttgtcccc ttccaatcag ccacttctga gaaccccat ctaacttcct actggaaaag       360
agggcctcct caggagcagt ccaagagttt tcaaagataa cgtgacaact accatctaga      420
ggaaagggtg caccctcagc agagaagccg agagcttaac tctggtcgtt ccagagaca       480
acctgctggc tgtcttggga tgcgcccagc ctttgagagg ccactacccc atgaacttct      540
gccatccact ggacatgaag ctgaggacac tgggcttcaa cactgagttg tcatgagagg      600
gacaggctct gccctcaagc cggctgaggg cagcaaccac tctcctcccc tttctcacgc      660
aaagccattc ccacaaatcc agaccatacc atgaagcaac gagacccaaa cagtttggct      720
caagaggata tgaggactgt ctcagcctgg ctttgggctg acaccatgca cacacacaag      780
gtccacttct aggttttcag cctagatggg agtcgtgt                              818
```

```
        <210> 228
        <211> 744
        <212> DNA
        <213> Homo sapien


        <400> 228
actggagaca ctgttgaact tgatcaagac ccagaccacc ccaggtctcc ttcgtgggat      60
gtcatgacgt ttgacatacc tttggaacga gcctcctcct tggaagatgg aagaccgtgt      120
tcgtggccga cctggcctct cctggcctgt ttcttaagat gcggagtcac atttcaatgg      180
taggaaaagt ggcttcgtaa aatagaagag cagtcactgt ggaactacca aatggcgaga      240
tgctcggtgc acattggggt gctttgggat aaaagattta tgagccaact attctctggc      300
accagattct aggccagttt gttccactga agcttttccc acagcagtcc acctctgcag      360
gctggcagct gaatggcttg ccggtggctc tgtggcaaga tcacactgag atcgatgggt      420
gagaaggcta ggatgcttgt ctagtgttct tagctgtcac gttggctcct tccaggttgg      480
ccagacggtg ttggccactc ccttctaaaa cacaggcgcc ctcctggtga cagtgacccg      540
ccgtggtatg ccttggccca ttccagcagt cccagttatg catttcaagt ttggggtttg      600
ttcttttcgt taatgttcct ctgtgttgtc agctgtcttc atttcctggg ctaagcagca      660
ttgggagatg tggaccagag atccactcct taagaaccag tggcgaaaga cactttcttt      720
cttcactctg aagtagctgg tggt                                            744
```

```
        <210> 229
        <211> 300
        <212> DNA
        <213> Homo sapien


        <400> 229
cgagtctggg ttttgtctat aaagtttgat ccctcctttt ctcatccaaa tcatgtgaac      60
cattacacat cgaaataaaa gaaaggtggc agacttgccc aacgccaggc tgacatgtgc      120
tgcagggttg ttgttttta attattattg ttagaaacgt cacccacagt ccctgttaat       180
ttgtatgtga cagccaactc tgagaaggtc ctattttttcc acctgcagag gatccagtct      240
cactaggctc ctccttgccc tcacactgga gtctccgcca gtgtgggtgc ccactgacat      300
```

```
        <210> 230
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 230
cagcagaaca aatacaaata tgaagagtgc aaagatctca taaaatctat gctgaggaat      60
gagcgacagt tcaaggagga gaagcttgca gagcagctca agcaagctga ggagctcagg      120
caatataaag tcctggttca cactcaggaa cgagagctga cccagttaag ggagaagttg      180
cgggaaggga gagatgcctc cctctcattg aatgagcatc tccaggccct cctcactccg      240
gatgaaccgg acaagtccca ggggcaggac ctccaagaaa cagacctcgg ccgcgaccac      300
g                                                                      301
```

80

```
<210> 231
<211> 301
<212> DNA
<213> Homo sapien

<400> 231
gcaagcacgc tggcaaatct ctgtcaggtc agctccagag aagccattag tcattttagc    60
caggaactcc aagtccacat ccttggcaac tggggacttg cgcaggttag ccttgaggat   120
ggcaacacgg gacttctcat caggaagtgg gatgtagatg agctgatcaa gacggccagg   180
tctgaggatg gcaggatcaa tgatgtcagg ccggttggta ccgccaatga tgaacacatt   240
ttttttgtg gacatgccat ccattctgt caggatctgg ttgatgactc ggtcagcagc     300
c                                                                    301


<210> 232
<211> 301
<212> DNA
<213> Homo sapien

<400> 232
agtaggtatt tcgtgagaag ttcaacacca aaactggaac atagttctcc ttcaagtgtt    60
ggcgacagcg gggcttcctg attctggaat ataactttgt gtaaattaac agccacctat   120
agaagagtcc atctgctgtg aaggagagac agagaactct gggttccgtc gtcctgtcca   180
cgtgctgtac caagtgctgg tgccagcctg ttacctgttc tcactgaaaa tctggctaat   240
gctcttgtgt atcacttctg attctgacaa tcaatcaatc aatggcctag agcactgact   300
g                                                                    301


<210> 233
<211> 301
<212> DNA
<213> Homo sapien

<400> 233
atgactgact tcccagtaag gctctctaag gggtaagtag gaggatccac aggatttgag    60
atgctaaggc cccagagatc gtttgatcca accctcttat tttcagaggg gaaaatgggg   120
cctagaagtt acagagcatc tagctggtgc gctggcaccc ctggcctcac acagactccc   180
gagtagctgg gactacaggc acacagtcac tgaagcaggc cctgttagca attctatgcg   240
tacaaattaa catgagatga gtagagactt tattgagaaa gcaagagaaa atcctatcaa   300
c                                                                    301


<210> 234
<211> 301
<212> DNA
<213> Homo sapien

<400> 234
aggtcctaca catcgagact catccatgat tgatatgaat ttaaaaatta caagcaaaga    60
cattttattc atcatgatgc tttcttttgt ttcttctttt cgttttcttc ttttttctttt   120
tcaatttcag caacatactt ctcaatttct tcaggattta aaatcttgag ggattgatct   180
cgcctcatga cagcaagttc aatgtttttg ccacctgact gaaccacttc caggagtgcc   240
ttgatcacca gcttaatggt cagatcatct gcttcaatgg cttcgtcagt atagttcttc   300
t                                                                    301


<210> 235
<211> 283
<212> DNA
<213> Homo sapien
```

81

```
        <400> 235
tggggctgtg catcaggcgg gtttgagaaa tattcaattc tcagcagaag ccagaatttg      60
aattccctca tcttttaggg aatcatttac caggtttgga gaggattcag acagctcagg     120
tgctttcact aatgtctctg aacttctgtc cctctttgtt catggatagt ccaataaata     180
atgttatctt tgaactgatg ctcataggag agaatataag aactctgagt gatatcaaca     240
ttagggattc aaagaaatat tagatttaag ctcacactgg tca                       283


        <210> 236
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 236
aggtcctcca ccaactgcct gaagcacggt taaaattggg aagaagtata gtgcagcata      60
aatactttta aatcgatcag atttccctaa cccacatgca atcttcttca ccagaagagg     120
tcggagcagc atcattaata ccaagcagaa tgcgtaatag ataaatacaa tggtatatag     180
tgggtagacg gcttcatgag tacagtgtac tgtggtatcg taatctggac ttgggttgta     240
aagcatcgtg taccagtcag aaagcatcaa tactcgacat gaacgaatat aaagaacacc     300
a                                                                      301


        <210> 237
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 237
cagtggtagt ggtggtggac gtggcgttgg tcgtggtgcc ttttttggtg cccgtcacaa      60
actcaatttt tgttcgctcc tttttggcct tttccaattt gtccatctca attttctggg     120
ccttggctaa tgcctcatag taggagtcct cagaccagcc atggggatca aacatatcct     180
ttgggtagtt ggtgccaagc tcgtcaatgg cacagaatgg atcagcttct cgtaaatcta     240
gggttccgaa attctttctt cctttggata atgtagttca tatccattcc ctcctttatc     300
t                                                                      301


        <210> 238
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 238
gggcaggttt tttttttttt tttttgatg gtgcagaccc ttgctttatt tgtctgactt       60
gttcacagtt cagccccctg ctcagaaaac caacgggcca gctaaggaga ggaggaggca     120
ccttgagact tccggagtcg aggctctcca gggttcccca gcccatcaat cattttctgc     180
accccctgcc tgggaagcag ctccctgggg ggtgggaatg ggtgactaga agggatttca     240
gtgtgggacc cagggtctgt tcttcacagt aggaggtgga agggatgact aatttctttta    300
t                                                                      301


        <210> 239
        <211> 239
        <212> DNA
        <213> Homo sapien


        <400> 239
ataagcagct agggaattct ttatttagta atgtcctaac ataaaagttc acataactgc      60
ttctgtcaaa ccatgatact gagctttgtg acaacccaga ataactaag agaaggcaaa      120
cataatacct tagagatcaa gaaacattta cacagttcaa ctgtttaaaa atagctcaac     180
attcagccag tgagtagagt gtgaatgcca gcatacacag tatacaggtc cttcaggga     239


        <210> 240
```

```
<211> 300
<212> DNA
<213> Homo sapien

<400> 240
ggtcctaatg aagcagcagc ttccacattt taacgcaggt ttacggtgat actgtccttt      60
gggatctgcc ctccagtgga accttttaag gaagaagtgg gcccaagcta agttccacat     120
gctgggtgag ccagatgact tctgttccct ggtcactttc ttcaatgggg cgaatggggg     180
ctgccaggtt tttaaaatca tgcttcatct tgaagcacac ggtcacttca ccctcctcac     240
gctgtgggtg tactttgatg aaaatacccca ctttgttggc ctttctgaag ctataatgtc    300


    <210> 241
    <211> 301
    <212> DNA
    <213> Homo sapien

    <400> 241
gaggtctggt gctgaggtct ctgggctagg aagaggagtt ctgtggagct ggaagccaga      60
cctctttgga ggaaactcca gcagctatgt tggtgtctct gagggaatgc aacaaggctg     120
ctcctccatg tattggaaaa ctgcaaactg gactcaactg gaaggaagtg ctgctgccag     180
tgtgaagaac cagcctgagg tgacagaaac ggaagcaaac aggaacagcc agtctttct     240
tcctcctcct gtcatacggt ctctctcaag catcctttgt tgtcaggggc ctaaaaggga    300
g                                                                     301


    <210> 242
    <211> 301
    <212> DNA
    <213> Homo sapien

    <400> 242
ccgaggtcct gggatgcaac caatcactct gtttcacgtg acttttatca ccatacaatt      60
tgtggcattt cctcattttc tacattgtag aatcaagagt gtaaataaat gtatatcgat     120
gtcttcaaga atatatcatt ccttttttcac tagaaccccat tcaaaatata agtcaagaat    180
cttaatatca acaaatatat caagcaaact ggaaggcaga ataactacca taatttagta     240
taagtaccca aagtttata aatcaaaagc cctaatgata accattttta gaattcaatc      300
a                                                                     301


    <210> 243
    <211> 301
    <212> DNA
    <213> Homo sapien

    <400> 243
aggtaagtcc cagtttgaag ctcaaaagat ctggtatgag cataggctca tcgacgacat      60
ggtggcccaa gctatgaaat cagagggagg cttcatctgg gcctgtaaaa actatgatgg     120
tgacgtgcag tcggactctg tggcccaagg gtatggctct ctcggcatga tgaccagcgt     180
gctggtttgt ccagatggca agacagtaga agcagaggct gcccacggga ctgtaacccg     240
tcactaccgc atgttccaga aaggacagga gacgtccacc aatcccattg cttccatttt     300
t                                                                     301


    <210> 244
    <211> 300
    <212> DNA
    <213> Homo sapien

    <400> 244
gctggtttgc aagaatgaaa tgaatgattc tacagctagg acttaacctt gaaatggaaa      60
gtcatgcaat cccatttgca ggatctgtct gtgcacatgc ctctgtagag agcagcattc     120
```

```
ccagggacct tggaaacagt tgacactgta aggtgcttgc tccccaagac acatcctaaa        180
aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc ccttcttatt tatgtgaaca        240
actgtttgtc ttttgtgtat ctttttttaaa ctgtaaagtt caattgtgaa aatgaatatc       300
```

        <210> 245
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 245

```
gtctgagtat ttaaaatgtt attgaaatta tccccaacca atgttagaaa agaaagaggt         60
tatatactta gataaaaaat gaggtgaatt actatccatt gaaatcatgc tcttagaatt       120
aaggccagga gatattgtca ttaatgtara cttcaggaca ctagagtata gcagccctat       180
gttttcaaag agcagagatg caattaaata ttgtttagca tcaaaaaggc cactcaatac       240
agctaataaa atgaaagacc taatttctaa agcaattctt tataatttac aaagttttaa       300
g                                                                        301
```

        <210> 246
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 246

```
ggtctgtcct acaatgcctg cttcttgaaa gaagtcggca ctttctagaa tagctaaata         60
acctgggctt attttaaaga actatttgta gctcagattg gttttcctat ggctaaaata       120
agtgcttctt gtgaaaatta aataaaacag ttaattcaaa gccttgatat atgttaccac       180
taacaatcat actaaatata ttttgaagta caaagtttga catgctctaa agtgacaacc       240
caaatgtgtc ttacaaaaca cgttcctaac aaggtatgct ttacactacc aatgcagaaa       300
c                                                                        301
```

        <210> 247
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 247

```
aggtcctttg gcagggctca tggatcagag ctcaaactgg agggaaaggc atttcgggta         60
gcctaagagg gcgactggcg gcagcacaac caaggaaggc aaggttgttt cccccacgct       120
gtgtcctgtg ttcaggtgcg acacacaatc ctcatgggaa caggatcacc catgcgctgc       180
ccttgatgat caaggttggg gcttaagtgg attaagggag gcaagttctg ggttccttgc       240
cttttcaaac catgaagtca ggctctgtat ccctcctttt cctaactgat attctaacta       300
a                                                                        301
```

        <210> 248
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 248

```
aggtccttgg agatgccatt tcagccgaag gactcttctw ttcggaagta caccctcact         60
attaggaaga ttcttagggg taattttct gaggaaggag aactagccaa cttaagaatt        120
acaggaagaa agtggtttgg aagacagcca agaaataaa agcagattaa attgtatcag        180
gtacattcca gcctgttggc aactccataa aaacatttca gattttaatc ccgaatttag       240
ctaatgagac tggatttttg tttttttatgt tgtgtgtcgc agagctaaaa actcagttcc       300
c                                                                        301
```

        <210> 249
        <211> 301

```
      <212> DNA
      <213> Homo sapien

      <400> 249
gtccagagga agcacctggt gctgaactag gcttgccctg ctgtgaactt gcacttggag        60
ccctgacgct gctgttctcc ccgaaaaacc cgaccgacct ccgcgatctc cgtcccgccc       120
ccagggagac acagcagtga ctcagagctg gtcgcacact gtgcctccct cctcaccgcc       180
catcgtaatg aattattttg aaaattaatt ccaccatcct ttcagattct ggatggaaag       240
actgaatctt tgactcagaa ttgtttgctg aaaagaatga tgtgactttc ttagtcattt       300
a                                                                       301


      <210> 250
      <211> 301
      <212> DNA
      <213> Homo sapien

      <400> 250
ggtctgtgac aaggacttgc aggctgtggg aggcaagtga cccttaacac tacacttctc        60
cttatcttta ttggcttgat aaacataatt atttctaaca ctagcttatt tccagttgcc       120
cataagcaca tcagtacttt tctctggctg gaatagtaaa ctaaagtatg gtacatctac       180
ctaaaagact actatgtgga ataatacata ctaatgaagt attacatgat ttaaagacta       240
caataaaacc aaacatgctt ataacattaa gaaaaacaat aaagatacat gattgaaacc       300
a                                                                       301


      <210> 251
      <211> 301
      <212> DNA
      <213> Homo sapien

      <400> 251
gccgaggtcc tacatttggc ccagtttccc cctgcatcct ctccagggcc cctgcctcat        60
agacaacctc atagagcata ggagaactgg ttgccctggg ggcagggggag ctgtctggat       120
ggcaggggtc ctcaaaaatg ccactgtcac tgccaggaaa tgcttctgag cagtacacct       180
cattgggatc aatgaaaagc ttcaagaaat cttcaggctc actctcttga aggcccggaa       240
cctctggagg ggggcagtgg aatcccagct ccaggacgga tcctgtcgaa aagatatcct       300
c                                                                       301


      <210> 252
      <211> 301
      <212> DNA
      <213> Homo sapien

      <400> 252
gcaaccaatc actctgtttc acgtgacttt tatcaccata caatttgtgg catttcctca        60
ttttctacat tgtagaatca agagtgtaaa taaatgtata tcgatgtctt caagaatata       120
tcattccttt ttcactagga acccattcaa aatataagtc aagaatctta atatcaacaa       180
atatatcaag caaactggaa ggcagaataa ctaccataat ttagtataag tacccaaagt       240
tttataaatc aaaagcccta atgataacca tttttagaat tcaatcatca ctgtagaatc       300
a                                                                       301


      <210> 253
      <211> 301
      <212> DNA
      <213> Homo sapien

      <400> 253
ttccctaaga agatgttatt ttgttgggtt ttgttccccc tccatctcga ttctcgtacc        60
caactaaaaa aaaaaaataa agaaaaaatg tgctgcgttc tgaaaaataa ctccttagct       120
```

```
tggtctgatt gttttcagac cttaaaatat aaacttgttt cacaagcttt aatccatgtg    180
gatttttttt cttagagaac cacaaaacat aaaaggagca agtcggactg aatacctgtt    240
tccatagtgc ccacagggta ttcctcacat tttctccata ggaaaatgct ttttcccaag    300
g                                                                     301
```

        <210> 254
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 254

```
cgctgcgcct ttcccttggg ggaggggcaa ggccagaggg ggtccaagtg cagcacgagg     60
aacttgacca attcccttga agcgggtggg ttaaaccctg taaatgggaa caaaatcccc    120
ccaaatctct tcatcttacc ctggtggact cctgactgta gaatttttg gttgaaacaa    180
gaaaaaaata aagctttgga ctttttcaagg ttgcttaaca ggtactgaaa gactggcctc    240
acttaaactg agccaggaaa agctgcagat ttattaatgg gtgtgttagt gtgcagtgcc    300
t                                                                     301
```

        <210> 255
        <211> 302
        <212> DNA
        <213> Homo sapien

        <400> 255

```
agctttttttt ttttttttttt ttttttttttt ttcattaaaa aatagtgctc tttattataa     60
attactgaaa tgtttctttt ctgaatataa atataaatat gtgcaaagtt tgacttggat    120
tgggattttg ttgagttctt caagcatctc ctaataccct caagggcctg agtaggggg    180
aggaaaaagg actggaggtg gaatctttat aaaaaacaag agtgattgag gcagattgta    240
aacattatta aaaaacaaga aacaaacaaa aaaatagaga aaaaaaccac cccaacacac    300
aa                                                                    302
```

        <210> 256
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 256

```
gttccagaaa acattgaagg tggcttccca aagtctaact agggataccc cctctagcct     60
aggaccctcc tccccacacc tcaatccacc aaaccatcca taatgcaccc agataggccc    120
accccaaaa gcctggacac cttgagcaca cagttatgac caggacagac tcatctctat    180
aggcaaatag ctgctggcaa actggcatta cctggtttgt ggggatgggg gggcaagtgt    240
gtggcctctc ggcctggtta gcaagaacat tcagggtagg cctaagttan tcgtgttagt    300
t                                                                     301
```

        <210> 257
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 257

```
gttgtggagg aactctggct tgctcattaa gtcctactga ttttcactat cccctgaatt     60
tccccactta ttttgtctt tcactatcgc aggccttaga agaggtctac ctgcctccag    120
tcttacctag tccagtctac cccctggagt tagaatggcc atcctgaagt gaaaagtaat    180
```

```
gtcacattac tcccttcagt gatttcttgt agaagtgcca atccctgaat gccaccaaga    240
tcttaatctt cacatcttta atcttatctc tttgactcct ctttacaccg gagaaggctc    300
c                                                                    301
```

        <210> 258
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 258
```
cagcagtagt agatgccgta tgccagcacg cccagcactc ccaggatcag caccagcacc    60
aggggcccag ccaccaggcg cagaagcaag ataaacagta ggctcaagac cagagccacc    120
cccagggcaa caagaatcca ataccaggac tgggcaaaat cttcaaagat cttaacactg    180
atgtctcggg cattgaggct gtcaataana cgctgatccc ctgctgtatg gtggtgtcat    240
tggtgatccc tgggagcgcc ggtggagtaa cgttggtcca tggaaagcag cgcccacaac    300
t                                                                    301
```

        <210> 259
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 259
```
tcatatatgc aaacaaatgc agactangcc tcaggcagag actaaaggac atctcttggg    60
gtgtcctgaa gtgatttgga cccctgaggg cagacaccta agtaggaatc ccagtgggaa    120
gcaaagccat aaggaagccc aggattcctt gtgatcagga agtgggccag gaaggtctgt    180
tccagctcac atctcatctg catgcagcac ggaccggatg cgcccactgg gtcttggctt    240
ccctcccatc ttctcaagca gtgtccttgt tgagccattt gcatccttgg ctccaggtgg    300
c                                                                    301
```

        <210> 260
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 260
```
ttttttttct ccctaaggaa aaagaaggaa caagtctcat aaaaccaaat aagcaatggt    60
aaggtgtctt aacttgaaaa agattaggag tcactggttt acaagttata attgaatgaa    120
agaactgtaa cagccacagt tggccatttc atgccaatgg cagcaaacaa caggattaac    180
tagggcaaaa taaataagtg tgtggaagcc ctgataagtg cttaataaac agactgattc    240
actgagacat cagtacctgc ccgggcggcc gctcgagccg aattctgcag atatccatca    300
c                                                                    301
```

        <210> 261
        <211> 301
        <212> DNA
        <213> Homo sapien

```
        <400> 261
aaatattcga gcaaatcctg taactaatgt gtctccataa aaggctttga actcagtgaa    60
tctgcttcca tccacgattc tagcaatgac ctctcggaca tcaaagctcc tcttaaggtt   120
agcaccaact attccataca attcatcagc aggaaataaa ggctcttcag aaggttcaat   180
ggtgacatcc aatttcttct gataatttag attcctcaca accttcctag ttaagtgaag   240
ggcatgatga tcatccaaag cccagtggtc acttactcca gactttctgc aatgaagatc   300
a                                                                   301


        <210> 262
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 262
gaggagagcc tgttacagca tttgtaagca cagaatactc caggagtatt tgtaattgtc    60
tgtgagcttc ttgccgcaag tctctcagaa atttaaaaag atgcaaatcc ctgagtcacc   120
cctagacttc ctaaaccaga tcctctgggg ctggaacctg gcactctgca tttgtaatga   180
gggctttctg gtgcacacct aattttgtgc atctttgccc taaatcctgg attagtgccc   240
catcattacc cccacattat aatgggatag attcagagca gatactctcc agcaaagaat   300
c                                                                   301


        <210> 263
        <211> 301
        <212> DNA
        <213> Homo sapien


        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G


        <400> 263
tttagcttgt ggtaaatgac tcacaaaact gattttaaaa tcaagttaat gtgaattttg    60
aaaattacta cttaatccta attcacaata acaatggcat taaggtttga cttgagttgg   120
ttcttagtat tatttatggt aaataggctc ttaccacttg caaataactg gccacatcat   180
taatgactga cttcccagta aggctctcta aggggtaagt angaggatcc acaggatttg   240
agatgctaag gccccagaga tcgtttgatc caaccctctt attttcagag gggaaaatgg   300
g                                                                   301


        <210> 264
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 264
aaagacgtta aaccactcta ctaccacttg tggaactctc aaagggtaaa tgacaaascc    60
aatgaatgac tctaaaaaca atatttacat ttaatggttt gtagacaata aaaaaacaag   120
gtggatagat ctagaattgt aacattttaa gaaaaccata scatttgaca gatgagaaag   180
ctcaattata gatgcaaagt tataactaaa ctactatagt agtaaagaaa tacatttcac   240
acccttcata taaattcact atcttggctt gaggcactcc ataaaatgta tcacgtgcat   300
a                                                                   301


        <210> 265
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 265
```

```
tgcccaagtt atgtgtaagt gtatccgcac ccagaggtaa aactacactg tcatctttgt        60
cttcttgtga cgcagtattt cttctctggg gagaagccgg gaagtcttct cctggctcta       120
catattcttg gaagtctcta atcaactttt gttccatttg tttcatttct tcaggaggga       180
ttttcagttt gtcaacatgt tctctaacaa cacttgccca tttctgtaaa gaatccaaag       240
cagtccaagg ctttgacatg tcaacaacca gcataactag agtatccttc agagatacgg       300
c                                                                        301
```

        <210> 266
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 266
```
taccgtctgc ccttcctccc atccaggcca tctgcgaatc tacatgggtc ctcctattcg        60
acaccagatc actctttcct ctacccacag gcttgctatg agcaagagac acaacctcct       120
ctcttctgtg ttccagcttc ttttcctgtt cttcccaccc cttaagttct attcctgggg       180
atagagacac caatacccat aacctctctc ctaagcctcc ttataaccca ggtgcacag       240
cacagactcc tgacaactgg taaggccaat gaactgggag ctcacagctg gctgtgcctg       300
a                                                                        301
```

        <210> 267
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 267
```
aaagagcaca ggccagctca gcctgccctg gccatctaga ctcagcctgg ctccatgggg        60
gttctcagtg ctgagtccat ccaggaaaag ctcacctaga ccttctgagg ctgaatcttc       120
atcctcacag gcagcttctg agagcctgat attcctagcc ttgatggtct ggagtaaagc       180
ctcattctga ttcctctcct tcttttcttt caagttggct ttcctcacat ccctctgttc       240
aattcgcttc agcttgtctg ctttagccct catttccaga agcttcttct ctttggcatc       300
t                                                                        301
```

        <210> 268
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 268
```
aatgtctcac tcaactactt cccagcctac cgtggcctaa ttctgggagt tttcttctta        60
gatcttggga gagctggttc ttctaaggag aaggaggaag gacagatgta actttggatc       120
tcgaagagga agtctaatgg aagtaattag tcaacggtcc ttgtttagac tcttggaata       180
tgctgggtgg ctcagtgagc ccttttggag aaagcaagta ttattcttaa ggagtaacca       240
cttcccattg ttctactttc taccatcatc aattgtatat tatgtattct ttggagaact       300
a                                                                        301
```

        <210> 269
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 269
```
taacaatata cactagctat cttttttaact gtccatcatt agcaccaatg aagattcaat       60
aaaattacct ttattcacac atctcaaaac aattctgcaa attcttagtg aagtttaact       120
atagtcacag accttaaata ttcacattgt tttctatgtc tactgaaaat aagttcacta       180
cttttctgga tattctttac aaaatcttat taaaattcct ggtattatca cccccaatta       240
tacagtagca caaccacctt atgtagtttt tacatgatag ctctgtagaa gtttcacatc       300
t                                                                        301
```

```
<210> 270
<211> 301
<212> DNA
<213> Homo sapien

<400> 270
cattgaagag cttttgcgaa acatcagaac acaagtgctt ataaaattaa ttaagcctta      60
cacaagaata catattcctt ttatttctaa ggagttaaac atagatgtag ctgatgtgga     120
gagcttgctg gtgcagtgca tattggataa cactattcat ggccgaattg atcaagtcaa     180
ccaactcctt gaactggatc atcagaagaa gggtggtgca cgatatactg cactagataa     240
tggaccaacc aactaaattc tctcaccagg ctgtatcagt aaactggctt aacagaaaac     300
a                                                                     301


<210> 271
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 271
aaaaggttct cataagatta acaatttaaa taaatatttg atagaacatt ctttctcatt      60
tttatagctc atctttaggg ttgatattca gttcatgctt cccttgctgt tcttgatcca     120
gaattgcaat cacttcatca gcctgtattc gctccaattc tctataaagt gggtccaagg     180
tgaaccacag agccacagca cacctctttc ccttggtgac tgccttcacc ccatganggt     240
tctctcctcc agatganaac tgatcatgcg cccacatttt gggtttttata gaagcagtca     300
c                                                                     301


<210> 272
<211> 301
<212> DNA
<213> Homo sapien

<400> 272
taaattgcta agccacagat aacaccaatc aaatggaaca aatcactgtc ttcaaatgtc      60
ttatcagaaa accaaatgag cctggaatct tcataatacc taaacatgcc gtatttagga     120
tccaataatt ccctcatgat gagcaagaaa aattctttgc gcacccctcc tgcatccaca     180
gcatcttctc caacaaatat aaccttgagt ggcttcttgt aatctatgtt ctttgttttc     240
ctaaggactt ccattgcatc tcctacaata ttttctctac gcaccactag aattaagcag     300
g                                                                     301


<210> 273
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 273
acatgtgtgt atgtgtatct ttgggaaaan aanaagacat cttgtttayt attttttttgg      60
agagangctg ggacatggat aatcacwtaa tttgctayta tyactttaat ctgactygaa     120
```

90

```
gaaccgtcta aaaataaaat ttaccatgtc dtatattcct tatagtatgc ttatttcacc     180
ttytttctgt ccagagagag tatcagtgac ananatttma gggtgaamac atgmattggt     240
gggacttnty tttacngagm accctgcccg sgcgccctcg makcngantt ccgcsananc     300
t                                                                     301
```

        <210> 274
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 274
```
cttatatact ctttctcaga ggcaaaagag gagatgggta atgtagacaa ttctttgagg     60
aacagtaaat gattattaga gagaangaat ggaccaagga gacagaaatt aacttgtaaa     120
tgattctctt tggaatctga atgagatcaa gaggccagct ttagcttgtg gaaaagtcca     180
tctaggtatg gttgcattct cgtcttcttt tctgcagtag ataatgaggt aaccgaaggc     240
aattgtgctt cttttgataa gaagctttct tggtcatatc aggaaattcc aganaaagtc     300
c                                                                     301
```

        <210> 275
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 275
```
tcggtgtcag cagcacgtgg cattgaacat tgcaatgtgg agcccaaacc acagaaaatg     60
gggtgaaatt ggccaacttt ctattaactt atgttggcaa ttttgccacc aacagtaagc     120
tggcccttct aataaaagaa aattgaaagg tttctcacta aacggaatta agtagtggag     180
tcaagagact cccaggcctc agcgtacctg cccgggcggc cgctcgaagc cgaattctgc     240
agatatccat cacactggcg gncgctcgan catgcatcta gaaggnccaa ttcgccctat     300
a                                                                     301
```

        <210> 276
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 276
```
tgtacacata ctcaataaat aaatgactgc attgtggtat tattactata ctgattatat     60
ttatcatgtg acttctaatt agaaaatgta tccaaaagca aaacagcaga tatacaaaat     120
taaagagaca gaagatagac attaacagat aaggcaactt atacattgag aatccaaatc     180
caatacattt aaacatttgg gaaatgaggg ggacaaatgg aagccagatc aaatttgtgt     240
aaaactattc agtatgtttc ccttgcttca tgtctgagaa ggctctcctt caatggggat     300
g                                                                     301
```

        <210> 277
        <211> 301
        <212> DNA
        <213> Homo sapien

```
        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 277
tttgttgatg tcagtatttt attacttgcg ttatgagtgc tcacctggga aattctaaag        60
atacagagga cttggaggaa gcagagcaac tgaatttaat ttaaaagaag gaaaacattg       120
gaatcatggc actcctgata ctttcccaaa tcaacactct caatgcccca ccctcgtcct       180
caccatagtg gggagactaa agtggccacg gatttgcctt angtgtgcag tgcgttctga       240
gttcnctgtc gattacatct gaccagtctc cttttttccga agtccntccg ttcaatcttg       300
c                                                                       301


        <210> 278
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G


        <400> 278
taccactaca ctccagcctg ggcaacagag caagacctgt ctcaaagcat aaaatggaat        60
aacatatcaa atgaaacagg gaaaatgaag ctgacaattt atggaagcca gggcttgtca       120
cagtctctac tgttattatg cattacctgg gaatttatat aagcccttaa taataatgcc       180
aatgaacatc tcatgtgtgc tcacaatgtt ctggcactat tataagtgct tcacaggttt       240
tatgtgttct tcgtaacttt atggantagg tactcggccg cgaacacgct aagccgaatt       300
c                                                                       301


        <210> 279
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G


        <400> 279
aaagcaggaa tgacaaagct tgcttttctg gtatgttcta ggtgtattgt gacttttact        60
gttatattaa ttgccaatat aagtaaatat agattatata tgtatagtgt ttcacaaagc       120
ttagaccttt accttccagc caccccacag tgcttgatat ttcagagtca gtcattggtt       180
atacatgtgt agttccaaag cacataagct agaanaanaa atatttctag ggagcactac       240
catctgtttt cacatgaaat gccacacaca tagaactcca acatcaattt cattgcacag       300
a                                                                       301


        <210> 280
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 280
ggtactggag ttttcctccc ctgtgaaaac gtaactactg ttgggagtga attgaggatg        60
tagaaaggtg gtggaaccaa attgtggtca atggaaatag gagaatatgg ttctcactct       120
```

```
tgagaaaaaa acctaagatt agcccaggta gttgcctgta acttcagttt ttctgcctgg      180
gtttgatata gtttagggtt ggggttagat taagatctaa attacatcag gacaaagaga      240
cagactatta actccacagt taattaagga ggtatgttcc atgtttattt gttaaagcag      300
t                                                                      301
```

        <210> 281
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 281
```
aggtacaaga aggggaatgg gaaagagctg ctgctgtggc attgttcaac ttggatattc       60
gccgagcaat ccaaatcctg aatgaagggg catcttctga aaaaggagat ctgaatctca      120
atgtggtagc aatggcttta tcgggttata cggatgagaa gaactccctt ggagagaaa      180
tgtgtagcac actgcgatta cagctaaata acccgtattt gtgtgtcatg tttgcatttc      240
tgacaagtga aacaggatct tacgatggag ttttgtatga aaacaaagtt gcagtacctc      300
g                                                                      301
```

        <210> 282
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 282
```
caggtactac agaattaaaa tactgacaag caagtagttt cttggcgtgc acgaattgca       60
tccagaaccc aaaaattaag aaattcaaaa agacattttg tgggcacctg ctagcacaga      120
agcgcagaag caaagcccag gcagaaccat gctaacctta cagctcagcc tgcacagaag      180
cgcagaagca aagcccaggc agaaccatgc taaccttaca gctcagcctg cacagaagcg      240
cagaagcaaa gcccaggcag aacatgctaa ccttacagct cagcctgcac agaagcacag      300
a                                                                      301
```

        <210> 283
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 283
```
atctgtatac ggcagacaaa ctttatarag tgtagagagg tgagcgaaag gatgcaaaag       60
cactttgagg gctttataat aatatgctgc ttgaaaaaaa aaatgtgtag ttgatactca      120
gtgcatctcc agacatagta aggggttgct ctgaccaatc aggtgatcat ttttctatc      180
acttcccagg ttttatgcaa aaattttgtt aaattctata atggtgatat gcatctttta      240
ggaaacatat acatttttaa aaatctattt tatgtaagaa ctgacagacg aatttgcttt      300
g                                                                      301
```

        <210> 284
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 284
```
caggtacaaa acgctattaa gtggcttaga atttgaacat ttgtggtctt tatttacttt       60
gcttcgtgtg tgggcaaagc aacatcttcc ctaaatatat attaccaaga aaagcaagaa      120
gcagattagg tttttgacaa aacaaacagg ccaaaggggg ctgacctgg agcagagcat      180
ggtgagaggc aaggcatgag agggcaagtt tgttgtggac agatctgtgc ctactttatt      240
actggagtaa aagaaaacaa agttcattga tgtcgaagga tatatacagt gttagaaatt      300
a                                                                      301
```

        <210> 285

```
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 285
acatcaccat gatcggatcc cccacccatt atacgttgta tgtttacata aatactcttc       60
aatgatcatt agtgttttaa aaaaaatact gaaaactcct tctgcatccc aatctctaac      120
caggaaagca aatgctattt acagacctgc aagccctccc tcaaacnaaa ctatttctgg      180
attaaatatg tctgacttct tttgaggtca cacgactagg caaatgctat ttacgatctg      240
caaaagctgt ttgaagagtc aaagccccca tgtgaacacg atttctggac cctgtaacag      300
t                                                                      301


        <210> 286
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 286
taccactgca ttccagcctg ggtgacagag tgagactccg tctccaaaaa aaactttgct       60
tgtatattat ttttgcctta cagtggatca ttctagtagg aaaggacagt aagatttttt      120
atcaaaatgt gtcatgccag taagagatgt tatattcttt tctcatttct tccccaccca      180
aaaataagct accatatagc ttataagtct caaatttttg ccttttacta aaatgtgatt      240
gtttctgttc attgtgtatg cttcatcacc tatattaggc aaattccatt ttttcccttg      300
t                                                                      301


        <210> 287
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 287
tacagatctg ggaactaaat attaaaaatg agtgtggctg gatatatgga gaatgttggg       60
cccagaagga acgtagagat cagatattac aacagctttg ttttgagggt tagaaatatg      120
aaatgatttg gttatgaacg cacagtttag gcagcagggc cagaatcctg accctctgcc      180
ccgtggttat ctcctcccca gcttggctgc ctcatgttat cacagtattc cattttgttt      240
gttgcatgtc ttgtgaagcc atcaagattt tctcgtctgt tttcctctca ttggtaatgc      300
t                                                                      301


        <210> 288
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 288
gtacacctaa ctgcaaggac agctgaggaa tgtaatgggc agccgctttt aaagaagtag       60
agtcaatagg aagacaaatt ccagttccag ctcagtctgg gtatctgcaa agctgcaaaa      120
gatctttaaa gacaatttca agagaatatt tccttaaagt tggcaatttg gagatcatac      180
aaaagcatct gcttttgtga tttaatttag ctcatctggc cactggaaga atccaaacag      240
tctgccttaa ttttggatga atgcatgatg gaaattcaat aatttagaaa gttaaaaaaa      300
a                                                                      301


        <210> 289
        <211> 301
```

```
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 289
ggtacactgt ttccatgtta tgtttctaca cattgctacc tcagtgctcc tggaaactta      60
gcttttgatg tctccaagta gtccaccttc atttaactct ttgaaactgt atcatctttg     120
ccaagtaaga gtggtggcct atttcagctg ctttgacaaa atgactggct cctgacttaa     180
cgttctataa atgaatgtgc tgaagcaaag tgcccatggt ggcggcgaan aagagaaaga     240
tgtgttttgt tttggactct ctgtggtccc ttccaatgct gtgggtttcc aaccagngga     300
a                                                                     301


<210> 290
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 290
acactgagct cttcttgata aatatacaga atgcttggca tatacaagat tctatactac      60
tgactgatct gttcatttct ctcacagctc ttaccccaa aagctttcc accctaagtg     120
ttctgacctc cttttctaat cacagtaggg atagaggcag anccacctac aatgaacatg     180
gagttctatc aagaggcaga aacagcacag aatcccagtt ttaccattcg ctagcagtgc     240
tgccttgaac aaaaacattt ctccatgtct cattttcttc atgcctcaag taacagtgag     300
a                                                                     301


<210> 291
<211> 301
<212> DNA
<213> Homo sapien

<400> 291
caggtaccaa tttcttctat cctagaaaca tttcattta tgttgttgaa acataacaac      60
tatatcagct agatttttt tctatgcttt acctgctatg gaaaatttga cacattctgc     120
tttactcttt tgtttatagg tgaatcacaa aatgtatttt tatgtattct gtagttcaat     180
agccatggct gtttacttca tttaatttat ttagcataaa gacattatga aaaggcctaa     240
acatgagctt cacttcccca ctaactaatt agcatctgtt atttcttaac cgtaatgcct     300
a                                                                     301


<210> 292
<211> 301
<212> DNA
<213> Homo sapien

<220>
<221> misc_feature
<222> (1)...(301)
<223> n = A,T,C or G

<400> 292
```

```
acctttttagt agtaatgtct aataataaat aagaaatcaa ttttataagg tccatatagc      60
tgtattaaat aattttttaag tttaaaagat aaaataccat cattttaaat gttggtattc     120
aaaaccaaag natataaccg aaaggaaaaa cagatgagac ataaaatgat ttgcnagatg     180
ggaaatatag tasttyatga atgttnatta aattccagtt ataatagtgg ctacacactc     240
tcactacaca cacagacccc acagtcctat atgccacaaa cacatttcca taacttgaaa     300
a                                                                       301
```

        <210> 293
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 293
```
ggtaccaagt gctggtgcca gcctgttacc tgttctcact gaaaagtctg gctaatgctc      60
ttgtgtagtc acttctgatt ctgacaatca atcaatcaat ggcctagagc actgactgtt     120
aacacaaacg tcactagcaa agtagcaaca gctttaagtc taaatacaaa gctgttctgt     180
gtgagaattt tttaaaaggc tacttgtata ataacccttg tcattttttaa tgtacctcgg     240
ccgcgaccac gctaagccga attctgcaga tatccatcac actggcggcc gctcgagcat     300
g                                                                       301
```

        <210> 294
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 294
```
tgacccataa caatatacac tagctatctt tttaactgtc catcattagc accaatgaag      60
attcaataaa attaccttta ttcacacatc tcaaaacaat tctgcaaatt cttagtgaag     120
tttaactata gtcacaganc ttaaatattc acattgtttt ctatgtctac tgaaaataag     180
ttcactactt ttctgggata ttctttacaa aatcttatta aaattcctgg tattatcacc     240
cccaattata cagtagcaca accaccttat gtagttttta catgatagct ctgtagaggt     300
t                                                                       301
```

        <210> 295
        <211> 305
        <212> DNA
        <213> Homo sapien

        <400> 295
```
gtactctttc tctcccctcc tctgaattta attctttcaa cttgcaattt gcaaggatta      60
cacatttcac tgtgatgtat attgtgttgc aaaaaaaaaa gtgtctttgt ttaaaattac     120
ttggtttgtg aatccatctt gctttttccc cattggaact agtcattaac ccatctctga     180
actggtagaa aaacrtctga agagctagtc tatcagcatc tgacaggtga attggatggt     240
tctcagaacc atttcacccca gacagcctgt ttctatcctg tttaataaat tagtttgggt     300
tctct                                                                   305
```

        <210> 296
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 296
```
aggtactatg ggaagctgct aaaataatat ttgatagtaa aagtatgtaa tgtgctatct      60
```

```
cacctagtag taaactaaaa ataaactgaa actttatgga atctgaagtt attttccttg    120
attaaataga attaataaac caatatgagg aaacatgaaa ccatgcaatc tactatcaac    180
tttgaaaaag tgattgaacg aaccacttag ctttcagatg atgaacactg ataagtcatt    240
tgtcattact ataaatttta aaatctgtta ataagatggc ctataggggag gaaaaagggg    300
c                                                                    301
```

        <210> 297
        <211> 300
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(300)
        <223> n = A,T,C or G

        <400> 297
```
actgagtttt aactggacgc caagcaggca aggctggaag gttttgctct ctttgtgcta     60
aaggttttga aaaccttgaa ggagaatcat tttgacaaga agtacttaag agtctagaga    120
acaaagangt gaaccagctg aaagctctcg ggggaanctt acatgtgttg ttaggcctgt    180
tccatcattg ggagtgcact ggccatccct caaaatttgt ctgggctggc ctgagtggtc    240
accgcacctc ggccgcgacc acgctaagcc gaattctgca gatatccatc acactggcgg    300
```

        <210> 298
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 298
```
tatggggttt gtcacccaaa agctgatgct gagaaaggcc tccctggggc ccctcccgcg     60
ggcatctgag agacctggtg ttccagtgtt tctggaaatg ggtcccagtg ccgccggctg    120
tgaagctctc agatcaatca cgggaagggc ctggcggtgg tggccacctg gaaccaccct    180
gtcctgtctg tttacatttc actaycaggt tttctctggg cattacnatt tgttcccta     240
caacagtgac ctgtgcattc tgctgtggcc tgctgtgtct gcaggtggct ctcagcgagg    300
t                                                                    301
```

        <210> 299
        <211> 301
        <212> DNA
        <213> Homo sapien

        <400> 299
```
gttttgagac ggagtttcac tcttgttgcc cagactggac tgcaatggca gggtctctgc     60
tcactgcacc ctctgcctcc caggttcgag caattctcct gcctcagcct cccaggtagc    120
tgggattgca ggctcacgcc accatacccca gctaattttt ttgtattttt agtagagacg    180
gagtttcgcc atgttggcca gctggtctca aactcctgac ctcaagcgac ctgcctgcct    240
cggcctccca aagtgctgga attataggca tgagtcaaca cgcccagcct aaagatattt    300
t                                                                    301
```

        <210> 300
        <211> 301
        <212> DNA
        <213> Homo sapien

```
        <400> 300
attcagtttt atttgctgcc ccagtatctg taaccaggag tgccacaaaa tcttgccaga      60
tatgtcccac acccactggg aaaggctccc acctggctac ttcctctatc agctgggtca     120
gctgcattcc acaaggttct cagcctaatg agtttcacta cctgccagtc tcaaaactta     180
gtaaagcaag accatgacat tcccccacgg aaatcagagt ttgccccacc gtcttgttac     240
tataaagcct gcctctaaca gtccttgctt cttcacacca atcccgagcg catcccccat     300
g                                                                     301


        <210> 301
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 301
ttaaattttt gagaggataa aaaggacaaa taatctagaa atgtgtcttc ttcagtctgc      60
agaggacccc aggtctccaa gcaaccacat ggtcaagggc atgaataatt aaaagttggt     120
gggaactcac aaagaccctc agagctgaga cacccacaac agtgggagct cacaaagacc     180
ctcagagctg agacacccac aacagtggga gctcacaaag accctcagag ctgagacacc     240
cacaacagca cctcgttcag ctgccacatg tgtgaataag gatgcaatgt ccagaagtgt     300
t                                                                     301


        <210> 302
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 302
aggtacacat ttagcttgtg gtaaatgact cacaaaactg attttaaaat caagttaatg      60
tgaattttga aaattactac ttaatcctaa ttcacaataa caatggcatt aaggtttgac     120
ttgagttggt cttagtatt atttatggta aataggctct taccacttgc aaataactgg     180
ccacatcatt aatgactgac ttcccagtaa ggctctctaa ggggtaagta ggaggatcca     240
caggatttga gatgctaagg ccccagagat cgtttgatcc aaccctctta ttttcagagg      300
g                                                                     301


        <210> 303
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 303
aggtaccaac tgtggaaata ggtagaggat cattttttct ttccatatca actaagttgt      60
atattgtttt ttgacagttt aacacatctt cttctgtcag agattctttc acaatagcac     120
tggctaatgg aactaccgct tgcatgttaa aaatggtggt ttgtgaaatg atcataggcc     180
agtaacgggt atgttttct aactgatctt ttgctcgttc caaagggacc tcaagacttc     240
catcgatttt atatctgggg tctagaaaag gagttaatct gttttccctc ataaattcac     300
c                                                                     301


        <210> 304
        <211> 301
        <212> DNA
        <213> Homo sapien


        <400> 304
acatggatgt tattttgcag actgtcaacc tgaatttgta tttgcttgac attgcctaat      60
tattagtttc agtttcagct tacccacttt ttgtctgcaa catgcaraas agacagtgcc     120
cttttttagtg tatcatatca ggaatcatct cacattggtt tgtgccatta ctggtgcagt     180
gactttcagc cacttgggta aggtggagtt ggccatatgt ctccactgca aaattactga     240
```

```
ttttcctttt gtaattaata agtgtgtgtg tgaagattct ttgagatgag gtatatatct        300
c                                                                         301
```

        <210> 305
        <211> 301
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(301)
        <223> n = A,T,C or G

        <400> 305
```
gangtacagc gtggtcaagg taacaagaag aaaaaaatgt gagtggcatc ctgggatgag        60
cagggggaca gacctggaca gacacgttgt catttgctgc tgtgggtagg aaaatgggcg        120
taaaggagga gaaacagata caaaatctcc aactcagtat taaggtattc tcatgcctag        180
aatattggta gaaacaagaa tacattcata tggcaaataa ctaaccatgg tggaacaaaa        240
ttctgggatt taagttggat accaangaaa ttgtattaaa agagctgttc atggaataag        300
a                                                                         301
```

        <210> 306
        <211> 8
        <212> PRT
        <213> Homo sapien

        <400> 306
Val Leu Gly Trp Val Ala Glu Leu
 1   5

        <210> 307
        <211> 637
        <212> DNA
        <213> Homo sapien

        <400> 307
```
acagggratg aagggaaagg gagaggatga ggaagccccc ctggggattt ggtttggtcc        60
ttgtgatcag gtggtctatg gggcttatcc ctacaaagaa gaatccagaa atagggggcac        120
attgaggaat gatacttgag cccaaagagc attcaatcat tgttttattt gccttmtttt        180
cacaccattg gtgagggagg gattaccacc ctggggttat gaagatggtt gaacacccca        240
cacatagcac cggagatatg agatcaacag tttcttagcc atagagattc acagcccaga        300
gcaggaggac gcttgcacac catgcaggat gacatggggg atgcgctcgg gattggtgtg        360
aagaagcaag gactgttaga ggcaggcttt atagtaacaa gacggtgggg caaactctga        420
tttccgtggg ggaatgtcat ggtcttgctt tactaagttt tgagactggc aggtagtgaa        480
actcattagg ctgagaacct tgtggaatgc acttgaccca sctgatagag gaagtagcca        540
ggtgggagcc tttcccagtg ggtgtgggac atatctggca agattttgtg gcactcctgg        600
ttacagatac tggggcagca aataaaactg aatcttg                                 637
```

        <210> 308
        <211> 647
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(647)
        <223> n = A,T,C or G

```
      <400> 308
acgattttca ttatcatgta aatcgggtca ctcaaggggc caaccacagc tgggagccac        60
tgctcagggg aaggttcata tgggactttc tactgcccaa ggttctatac aggatataaa       120
ggngcctcac agtatagatc tggtagcaaa gaagaagaaa caaacactga tctctttctg       180
ccacccctct gacccctttgg aactcctctg acccttaga acaagcctac ctaatatctg        240
ctagagaaaa gaccaacaac ggcctcaaag gatctcttac catgaaggtc tcagctaatt       300
cttggctaag atgtgggttc cacattaggt tctgaatatg gggggaaggg tcaatttgct       360
cattttgtgt gtggataaag tcaggatgcc caggggccag agcaggggggc tgcttgcttt      420
gggaacaatg gctgagcata taaccatagg ttatggggaa caaaacaaca tcaaagtcac       480
tgtatcaatt gccatgaaga cttgagggac ctgaatctac cgattcatct taaggcagca       540
ggaccagttt gagtggcaac aatgcagcag cagaatcaat ggaaacaaca gaatgattgc       600
aatgtccttt tttttctcct gcttctgact tgataaaagg ggaccgt                     647

      <210> 309
      <211> 460
      <212> DNA
      <213> Homo sapien


      <400> 309
actttatagt ttaggctgga cattggaaaa aaaaaaaagc cagaacaaca tgtgatagat        60
aatatgattg gctgcacact tccagactga tgaatgatga acgtgatgga ctattgtatg       120
gagcacatct tcagcaagag ggggaaatac tcatcatttt tggccagcag ttgtttgatc       180
accaaacatc atgccagaat actcagcaaa ccttcttagc tcttgagaag tcaaagtccg       240
ggggaattta ttcctggcaa tttttaattgg actccttatg tgagagcagc ggctacccag      300
ctggggtggt ggagcgaacc cgtcactagt ggacatgcag tggcagagct cctggtaacc       360
acctagagga atacacaggc acatgtgtga tgccaagcgt gacacctgta gcactcaaat       420
ttgtcttgtt tttgtctttc ggtgtgtaag attcttaagt                              460

      <210> 310
      <211> 539
      <212> DNA
      <213> Homo sapien


      <400> 310
acgggactta tcaaataaag ataggaaaag aagaaaactc aaatattata ggcagaaatg        60
ctaaaggttt taaatatgt caggattgga agaaggcatg gataaagaac aaagttcagt        120
taggaaagag aaacacagaa ggaagagaca caataaaagt cattatgtat tctgtgagaa       180
gtcagacagt aagatttgtg ggaaatgggt tggtttgttg tatggtatgt attttagcaa       240
taatctttat ggcagagaaa gctaaaatcc tttagcttgc gtgaatgatc acttgctgaa       300
ttcctcaagg taggcatgat gaaggagggt ttagaggaga cacagacaca atgaactgac       360
ctagatagaa agccttagta tactcagcta ggaatagtga ttctgagggc acactgtgac       420
atgattatgt cattacatgt atggtagtga tggggatgat aggaaggaag aacttatggc       480
atattttcac ccccacaaaa gtcagttaaa tattgggaca ctaaccatcc aggtcaaga        539

      <210> 311
      <211> 526
      <212> DNA
      <213> Homo sapien

      <220>
      <221> misc_feature
      <222> (1)...(526)
      <223> n = A,T,C or G

      <400> 311
caaatttgag ccaatgacat agaattttac aaatcaagaa gcttattctg gggccatttc        60
ttttgacgtt ttctctaaac tactaagag gcattaatga tccataaatt atattatcta       120
catttacagc atttaaaatg tgttcagcat gaaatattag ctacagggga agctaaataa       180
```

```
attaaacatg gaataaagat ttgtccttaa atataatcta caagaagact ttgatatttg     240
ttttcacaa gtgaagcatt cttataaagt gtcataacct ttttggggaa actatgggaa     300
aaaatgggga aactctgaag ggttttaagt atcttacctg aagctacaga ctccataacc     360
tctctttaca gggagctcct gcagcccta cagaaatgag tggctgagat tcttgattgc     420
acagcaagag cttctcatct aaaccctttc ccttttagt atctgtgtat caagtataaa     480
agttctataa actgtagtnt acttattta atccccaaag cacagt                    526
```

```
        <210> 312
        <211> 500
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(500)
        <223> n = A,T,C or G

        <400> 312
cctctctctc cccacccct gactctagag aactgggttt tctcccagta ctccagcaat     60
tcatttctga aagcagttga gccactttat tccaaagtac actgcagatg ttcaaactct     120
ccatttctct ttccctccca cctgccagtt ttgctgactc tcaacttgtc atgagtgtaa     180
gcattaagga cattatgctt cttcgattct gaagacaggc cctgctcatg gatgactctg     240
gcttcttagg aaaatatttt tcttccaaaa tcagtaggaa atctaaactt atccctctct     300
tgcagatgtc tagcagcttc agacatttgg ttaagaaccc atgggaaaaa aaaaaatcct     360
tgctaatgtg gtttcctttg taaaccanga ttcttatttg nctggtatag aatatcagct     420
ctgaacgtgt ggtaaagatt tttgtgtttg aatataggag aaatcagttt gctgaaaagt     480
tagtcttaat tatctattgg                                                 500
```

```
        <210> 313
        <211> 718
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(718)
        <223> n = A,T,C or G

        <400> 313
ggagatttgt gtggtttgca gccgagggag accaggaaga tctgcatggt gggaaggacc     60
tgatgataca gaggtgagaa ataagaaagg ctgctgactt taccatctga ggccacacat     120
ctgctgaaat ggagataatt aacatcacta gaaacagcaa gatgacaata taatgtctaa     180
gtagtgacat gtttttgcac atttccagcc cttttaaata tccacacaca caggaagcac     240
aaaaggaagc acagagatcc ctgggagaaa tgcccggccg ccatcttggg tcatcgatga     300
gcctcgccct gtgcctgntc ccgcttgtga gggaaggaca ttagaaaatg aattgatgtg     360
ttccttaaag gatggcagga aaacagatcc tgttgtggat atttatttga acgggattac     420
agatttgaaa tgaagtcaca aagtgagcat taccaatgag aggaaaacag acgagaaaat     480
cttgatggtt cacaagacat gcaacaaaca aaatggaata ctgtgatgac acgagcagcc     540
aactggggag gagataccac ggggcagagg tcaggattct ggccctgctg cctaactgtg     600
cgttatacca atcatttcta tttctaccct caaacaagct gtngaatatc tgacttacgg     660
ttcttntggc ccacattttc atnatccacc ccntcntttt aanntttantc caaantgt     718
```

```
        <210> 314
        <211> 358
        <212> DNA
        <213> Homo sapien

        <400> 314
```

```
gtttatttac attacagaaa aaacatcaag acaatgtata ctatttcaaa tatatccata      60
cataatcaaa tatagctgta gtacatgttt tcattggtgt agattaccac aaatgcaagg     120
caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg tgtagtccaa     180
gctctcggta gtccagccac tgtgaaacat gctcccttta gattaacctc gtggacgctc     240
ttgttgtatt gctgaactgt agtgccctgt attttgcttc tgtctgtgaa ttctgttgct     300
tctggggcat ttccttgtga tgcagaggac caccacacag atgacagcaa tctgaatt      358
```

        <210> 315
        <211> 341
        <212> DNA
        <213> Homo sapien

        <400> 315
```
taccacctcc ccgctggcac tgatgagccg catcaccatg gtcaccagca ccatgaaggc      60
ataggtgatg atgaggacat ggaatgggcc cccaaggatg gtctgtccaa agaagcgagt     120
gaccccccatt ctgaagatgt ctggaacctc taccagcagg atgatgatag ccccaatgac     180
agtcaccagc tccccgacca gccggatatc gtccttaggg gtcatgtagg cttcctgaag     240
tagcttctgc tgtaagaggg tgttgtcccg ggggctcgtg cggttattgg tcctgggctt     300
gaggggcgg tagatgcagc acatggtgaa gcagatgatg t     341
```

        <210> 316
        <211> 151
        <212> DNA
        <213> Homo sapien

        <400> 316
```
agactgggca agactcttac gccccacact gcaatttggt cttgttgccg tatccatttta      60
tgtgggcctt tctcgagttt ctgattataa acaccactgg agcgatgtgt tgactggact     120
cattcaggga gctctggttg caatattagt t     151
```

        <210> 317
        <211> 151
        <212> DNA
        <213> Homo sapien

        <400> 317
```
agaactagtg gatcctaatg aaatacctga aacatatatt ggcatttatc aatggctcaa      60
atcttcattt atctctggcc ttaaccctgg ctcctgaggc tgcggccagc agatcccagg     120
ccagggctct gttcttgcca cacctgcttg a     151
```

        <210> 318
        <211> 151
        <212> DNA
        <213> Homo sapien

        <400> 318
```
actggtggga ggcgctgttt agttggctgt tttcagaggg gtctttcgga gggacctcct      60
gctgcaggct ggagtgtctt tattcctggc gggagaccgc acattccact gctgaggctg     120
tgggggcggt ttatcaggca gtgataaaca t     151
```

        <210> 319
        <211> 151
        <212> DNA
        <213> Homo sapien

        <400> 319
```
aactagtgga tccagagcta taggtacagt gtgatctcag ctttgcaaac acattttcta      60
catagatagt actaggtatt aatagatatg taaagaaaga aatcacacca ttaataatgg     120
```

```
taagattggg tttatgtgat tttagtgggt a                              151


    <210> 320
    <211> 150
    <212> DNA
    <213> Homo sapien


    <400> 320
aactagtgga tccactagtc cagtgtggtg gaattccatt gtgttggggt tctagatcgc    60
gagcggctgc ccttttttttt tttttttttg ggggggaatt ttttttttttt aatagttatt   120
gagtgttcta cagcttacag taaataccat                                     150


    <210> 321
    <211> 151
    <212> DNA
    <213> Homo sapien


    <400> 321
agcaactttg tttttcatcc aggttatttt aggcttagga tttcctctca cactgcagtt    60
tagggtggca ttgtaaccag ctatggcata ggtgttaacc aaaggctgag taaacatggg   120
tgcctctgag aaatcaaagt cttcatacac t                                   151


    <210> 322
    <211> 151
    <212> DNA
    <213> Homo sapien


    <220>
    <221> misc_feature
    <222> (1)...(151)
    <223> n = A,T,C or G


    <400> 322
atccagcatc ttctcctgtt tcttgccttc cttttttcttc ttcttasatt ctgcttgagg    60
tttgggcttg gtcagtttgc cacagggctt ggagatggtg acagtcttct ggcattcggc   120
attgtgcagg gctcgcttca nacttccagt t                                   151


    <210> 323
    <211> 151
    <212> DNA
    <213> Homo sapien


    <220>
    <221> misc_feature
    <222> (1)...(151)
    <223> n = A,T,C or G


    <400> 323
tgaggacttg tkttcttttt ctttattttt aatcctctta ckttgtaaat atattgccta    60
nagactcant tactacccag tttgtggttt twtgggagaa atgtaactgg acagttagct   120
gttcaatyaa aaagacactt ancccatgtg g                                   151


    <210> 324
    <211> 461
    <212> DNA
    <213> Homo sapien


    <220>
```

```
<221> misc_feature
<222> (1)...(461)
<223> n = A,T,C or G

<400> 324
acctgtgtgg aatttcagct ttcctcatgc aaaaggattt tgtatccccg gcctacttga     60
agaagtggtc agctaaagga atccaggttg ttggttggac tgttaatacc tttgatgaaa    120
agagttacta cgaatcccat cttggttcca gctatatcac tgacagcatg gtagaagact    180
gcgaacctca cttctagact ttcacggtgg gacgaaacgg gttcagaaac tgccaggggc    240
ctcatacagg gatatcaaaa taccctttgt gctacccagg ccctggggaa tcaggtgact    300
cacacaaatg caatagttgg tcactgcatt tttacctgaa ccaaagctaa acccggtgtt    360
gccaccatgc accatggcat gccagagttc aacactgttg ctcttgaaaa ttgggtctga    420
aaaaacgcac aagagcccct gccctgccct agctgangca c                       461


<210> 325
<211> 400
<212> DNA
<213> Homo sapien

<400> 325
acactgtttc catgttatgt ttctacacat tgctacctca gtgctcctgg aaacttagct     60
tttgatgtct ccaagtagtc caccttcatt taactctttg aaactgtatc atctttgcca    120
agtaagagtg gtggcctatt tcagctgctt tgacaaaatg actggctcct gacttaacgt    180
tctataaatg aatgtgctga agcaaagtgc ccatggtggc ggcgaagaag agaaagatgt    240
gttttgtttt ggactctctg tggtcccttc caatgctgtg ggtttccaac caggggaagg    300
gtcccttttg cattgccaag tgccataacc atgagcacta cgctaccatg gttctgcctc    360
ctggccaagc aggctggttt gcaagaatga aatgaatgat                          400


<210> 326
<211> 1215
<212> DNA
<213> Homo sapien

<400> 326
ggaggactgc agcccgcact cgcagccctg gcaggcggca ctggtcatgg aaaacgaatt     60
gttctgctcg ggcgtcctgg tgcatccgca gtgggtgctg tcagccgcac actgtttcca    120
gaactcctac accatcgggc tgggcctgca cagtcttgag gccgaccaag agccagggag    180
ccagatggtg gaggccagcc tctccgtacg gcacccagag tacaacagac ccttgctcgc    240
taacgacctc atgctcatca agttggacga atccgtgtcc gagtctgaca ccatccggag    300
catcagcatt gcttcgcagt gccctaccgc ggggaactct tgcctcgttt ctggctgggg    360
tctgctggcg aacggcagaa tgcctaccgt gctgcagtgc gtgaacgtgt cggtggtgtc    420
tgaggaggtc tgcagtaagc tctatgaccc gctgtaccac cccagcatgt tctgcgccgg    480
cggagggcaa gaccagaagg actcctgcaa cggtgactct gggggggcccc tgatctgcaa    540
cgggtacttg cagggccttg tgtctttcgg aaaagccccg tgtggccaag ttggcgtgcc    600
aggtgtctac accaacctct gcaaattcac tgagtggata gagaaaaccg tccaggccag    660
ttaactctgg ggactgggaa cccatgaaat tgacccccaa atacatcctg cggaaggaat    720
tcaggaatat ctgttcccag cccctcctcc ctcaggccca ggagtccagg cccccagccc    780
ctcctccctc aaaccaaggg tacagatccc cagcccctcc tccctcagac caggagtcc    840
agacccccca gcccctcctc cctcagaccc aggagtccag cccctcctcc ctcagaccca    900
ggagtccaga cccccagcc cctcctccct cagacccagg gtccaggcc cccaacccct    960
cctccctcag actcagaggt ccaagccccc aaccccctcct tccccagacc cagaggtcca   1020
ggtcccagcc cctcctccct cagacccagc ggtccaatgc cacctagact ctccctgtac   1080
acagtgcccc cttgtggcac gttgacccaa ccttaccagt tggttttttca tttttttgtcc  1140
ctttcccctta gatccagaaa taaagtctaa gagaagcgca aaaaaaaaa aaaaaaaaa    1200
aaaaaaaaa aaaaa                                                      1215


<210> 327
<211> 220
```

<210> PRT
<213> Homo sapien

<400> 327
Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met
1   5   10   15
Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val
            20   25   30
Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly
        35   40   45
Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu
    50   55   60
Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu Leu Ala
65   70   75   80
Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu Ser Asp
                85   90   95
Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala Gly Asn
            100   105   110
Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg Met Pro
        115   120   125
Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu Val Cys
    130   135   140
Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys Ala Gly
145   150   155   160
Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly Gly Pro
                165   170   175
Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly Lys Ala
                180   185   190
Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu Cys Lys
        195   200   205
Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
    210   215   220

<210> 328
<211> 234
<212> DNA
<213> Homo sapien

<400> 328
cgctcgtctc tggtagctgc agccaaatca taaacggcga ggactgcagc ccgcactcgc   60
agccctggca ggcggcactg gtcatggaaa acgaattgtt ctgctcgggc gtcctggtgc   120
atccgcagtg ggtgctgtca gccacacact gtttccagaa ctcctacacc atcgggctgg   180
gcctgcacag tcttgaggcc gaccaagagc cagggagcca gatggtggag gcca   234

<210> 329
<211> 77
<212> PRT
<213> Homo sapien

<400> 329
Leu Val Ser Gly Ser Cys Ser Gln Ile Ile Asn Gly Glu Asp Cys Ser
1   5   10   15
Pro His Ser Gln Pro Trp Gln Ala Ala Leu Val Met Glu Asn Glu Leu
            20   25   30
Phe Cys Ser Gly Val Leu Val His Pro Gln Trp Val Leu Ser Ala Thr
        35   40   45
His Cys Phe Gln Asn Ser Tyr Thr Ile Gly Leu Gly Leu His Ser Leu
    50   55   60

Glu Ala Asp Gln Glu Pro Gly Ser Gln Met Val Glu Ala
65   70   75

               <210> 330
               <211> 70
               <212> DNA
               <213> Homo sapien

               <400> 330

cccaacacaa tggcccgatc ccatccctga ctccgccctc aggatcgctc gtctctggta   60
gctgcagcca   70

               <210> 331
               <211> 22
               <212> PRT
               <213> Homo sapien

               <400> 331
Gln His Asn Gly Pro Ile Pro Ser Leu Thr Pro Pro Ser Gly Ser Leu
 1   5   10   15
Val Ser Gly Ser Cys Ser
       20

               <210> 332
               <211> 2507
               <212> DNA
               <213> Homo sapien

               <400> 332
tggtgccgct gcagccggca gagatggttg agctcatgtt cccgctgttg ctcctccttc   60
tgcccttcct tctgtatatg gctgcgcccc aaatcaggaa aatgctgtcc agtggggtgt   120
gtacatcaac tgttcagctt cctgggaaag tagttgtggt cacaggagct aatacaggta   180
tcgggaagga gacagccaaa gagctggctc agagaggagc tcgagtatat ttagcttgcc   240
gggatgtgga aaaggggaa ttggtggcca aagagatcca gaccacgaca gggaaccagc   300
aggtgttggt gcggaaactg gacctgtctg atactaagtc tattcgagct tttgctaagg   360
gcttcttagc tgaggaaaag caccctccacg ttttgatcaa caatgcagga gtgatgatgt   420
gtccgtactc gaagacagca gatggctttg agatgcacat aggagtcaac cacttgggtc   480
acttcctcct aacccatctg ctgctagaga aactaaagga atcagcccca tcaaggatag   540
taaatgtgtc ttccctcgca catcacctgg gaaggatcca cttccataac ctgcagggcg   600
agaaattcta caatgcaggc ctggcctact gtcacagcaa gctagccaac atcctcttca   660
cccaggaact ggcccggaga ctaaaaggct ctggcgttac gacgtattct gtacaccctg   720
gcacagtcca atctgaactg gttcggcact catctttcat gagatggatg tggtggcttt   780
tctccttttt catcaagact cctcagcagg gagcccagac cagcctgcac tgtgccttaa   840
cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg gcatgggtct   900
ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt tgtgacctgc   960
tgggcctccc aatagactaa caggcagtgc cagttggacc caagagaaga ctgcagcaga   1020
ctacacagta cttcttgtca aaatgattct ccttcaaggt tttcaaaacc tttagcacaa   1080
agagagcaaa accttccagc cttgcctgct tggtgtccag ttaaaactca gtgtactgcc   1140
agattcgtct aaatgtctgt catgtccaga tttactttgc ttctgttact gccagagtta   1200
ctagagatat cataatagga taagaagacc ctcatatgac ctgcacagct cattttcctt   1260
ctgaaagaaa ctactaccta ggagaatcta agctatagca gggatgattt atgcaaattt   1320
gaactagctt ctttgttcac aattcagttc ctcccaacca accagtcttc acttcaagag   1380
ggccacactg caacctcagc ttaacatgaa taacaaagac tggctcagga gcagggcttg   1440
cccaggcatg gtggatcacc ggaggtcagt agttcaagac cagcctggcc aacatggtga   1500
aaccccacct ctactaaaaa ttgtgtatat ctttgtgtgt cttcctgttt atgtgtgcca   1560
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        <212> DNA
        <213> Homo sapien

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        <212> DNA
        <213> Homo sapien

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        <211> 2984
        <212> DNA
        <213> Homo sapien

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        <212> PRT
        <213> Homo sapien


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Leu Asp Ser Glu Asn Thr Ser Gly Ala Leu Pro Arg Leu Pro Gln Thr
            20                  25                  30
Pro Lys Gln Pro Gln Lys Arg Ser Arg Ala Ala Phe Ser His Thr Gln
        35                  40                  45
Val Ile Glu Leu Glu Arg Lys Phe Ser His Gln Lys Tyr Leu Ser Ala
        50                  55                  60
Pro Glu Arg Ala His Leu Ala Lys Asn Leu Lys Leu Thr Glu Thr Gln
65                  70                  75                  80
Val Lys Ile Trp Phe Gln Asn Arg Arg Tyr Lys Thr Lys Arg Lys Gln
                85                  90                  95
Leu Ser Ser Glu Leu Gly Asp Leu Glu Lys His Ser Ser Leu Pro Ala
            100                 105                 110
Leu Lys Glu Glu Ala Phe Ser Arg Ala Ser Leu Val Ser Val Tyr Asn
        115                 120                 125
Ser Tyr Pro Tyr Tyr Pro Tyr Leu Tyr Cys Val Gly Ser Trp Ser Pro
    130                 135                 140
Ala Phe Trp
145


        <210> 337
        <211> 9
        <212> PRT
        <213> Homo sapien


        <400> 337
Ala Leu Thr Gly Phe Thr Phe Ser Ala
 1               5


        <210> 338
        <211> 9
        <212> PRT
        <213> Homo sapien


        <400> 338
Leu Leu Ala Asn Asp Leu Met Leu Ile
 1               5


        <210> 339
        <211> 318
        <212> PRT
        <213> Homo sapien


        <400> 339
Met Val Glu Leu Met Phe Pro Leu Leu Leu Leu Leu Pro Phe Leu
 1               5                   10                  15
Leu Tyr Met Ala Ala Pro Gln Ile Arg Lys Met Leu Ser Ser Gly Val
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```
                    20                    25                    30
Cys Thr Ser Thr Val Gln Leu Pro Gly Lys Val Val Val Thr Gly
        35                    40                    45
Ala Asn Thr Gly Ile Gly Lys Glu Thr Ala Lys Glu Leu Ala Gln Arg
    50                    55                    60
Gly Ala Arg Val Tyr Leu Ala Cys Arg Asp Val Glu Lys Gly Glu Leu
65                    70                    75                    80
Val Ala Lys Glu Ile Gln Thr Thr Thr Gly Asn Gln Gln Val Leu Val
            85                    90                    95
Arg Lys Leu Asp Leu Ser Asp Thr Lys Ser Ile Arg Ala Phe Ala Lys
            100                   105                   110
Gly Phe Leu Ala Glu Glu Lys His Leu His Val Leu Ile Asn Asn Ala
        115                   120                   125
Gly Val Met Met Cys Pro Tyr Ser Lys Thr Ala Asp Gly Phe Glu Met
    130                   135                   140
His Ile Gly Val Asn His Leu Gly His Phe Leu Leu Thr His Leu Leu
145                   150                   155                   160
Leu Glu Lys Leu Lys Glu Ser Ala Pro Ser Arg Ile Val Asn Val Ser
                165                   170                   175
Ser Leu Ala His His Leu Gly Arg Ile His Phe His Asn Leu Gln Gly
                180                   185                   190
Glu Lys Phe Tyr Asn Ala Gly Leu Ala Tyr Cys His Ser Lys Leu Ala
        195                   200                   205
Asn Ile Leu Phe Thr Gln Glu Leu Ala Arg Arg Leu Lys Gly Ser Gly
    210                   215                   220
Val Thr Thr Tyr Ser Val His Pro Gly Thr Val Gln Ser Glu Leu Val
225                   230                   235                   240
Arg His Ser Ser Phe Met Arg Trp Met Trp Trp Leu Phe Ser Phe Phe
                245                   250                   255
Ile Lys Thr Pro Gln Gln Gly Ala Gln Thr Ser Leu His Cys Ala Leu
        260                   265                   270
Thr Glu Gly Leu Glu Ile Leu Ser Gly Asn His Phe Ser Asp Cys His
        275                   280                   285
Val Ala Trp Val Ser Ala Gln Ala Arg Asn Glu Thr Ile Ala Arg Arg
    290                   295                   300
Leu Trp Asp Val Ser Cys Asp Leu Leu Gly Leu Pro Ile Asp
305                   310                   315
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<212> DNA
<213> Homo sapien

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tgctcaatct cgccattcga ctcttgctcc aaactgtatg aagacacctg actgcacgtt       420
ttttctgggc ttccagaatt taaagtgaaa ggcagcactc ctaagctccg actccgatgc       480
ctg                                                                       483
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<210> 341
<211> 344
<212> DNA
<213> Homo sapien
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gctgccttac aagtattaaa tattttactt ctttccataa agagtagctc aaaatatgca       180
attaatttaa taatttctga tgatggtttt atctgcagta atatgtatat catctattag       240
aatttactta atgaaaaact gaagagaaca aaatttgtaa ccactagcac ttaagtactc       300
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        <212> DNA
        <213> Homo sapien
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cctggcaggt aaaccaatgc caagagagtg atggaaacca ttggcaagac tttgttgatg       180
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        <211> 382
        <212> DNA
        <213> Homo sapien
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cttgtaactc tcctttctcc tttcttcccc tttctctgcc cgcctttccc atcctgctgt       180
agacttcttg attgtcagtc tgtgtcacat ccagtgattg ttttggtttc tgttcccttt       240
ctgactgccc aaggggctca gaaccccagc aatcccttcc tttcactacc ttctttttg        300
ggggtagttg gaagggactg aaattgtggg gggaaggtag gaggcacatc aataaagagg       360
aaaccaccaa gctgaaaaaa aa                                                 382
```

```
        <210> 344
        <211> 536
        <212> DNA
        <213> Homo sapien
```

```
        <400> 344
ctgggcctga agctgtaggg taaatcagag gcaggcttct gagtgatgag agtcctgaga        60
caataggcca cataaacttg ctggatgga acctcacaat aaggtggtca cctcttgttt        120
gtttaggggg atgccaagga taaggccagc tcagttatat gaagagaagc agaacaaaca       180
agtctttcag agaaatggat gcaatcagag tgggatcccg gtcacatcaa ggtcacactc       240
caccttcatg tgcctgaatg gttgccaggt cagaaaaatc caccccttac gagtgcggct       300
tcgaccctat atcccccgcc cgcgtccctt tctccataaa attcttctta gtagctatta       360
ccttcttatt atttgatcta gaaattgccc tccttttacc cctaccatga gccctacaaa       420
caactaacct gccactaata gttatgtcat ccctcttatt aatcatcatc ctagccctaa       480
gtctggccta tgagtgacta caaaaaggat tagactgagc cgaataacaa aaaaaa           536
```

```
        <210> 345
        <211> 251
```

```
        <212> DNA
        <213> Homo sapien

        <400> 345
accttttgag gtctctctca ccacctccac agccaccgtc accgtgggat gtgctggatg        60
tgaatgaagc ccccatcttt gtgcctcctg aaaagagagt ggaagtgtcc gaggactttg       120
gcgtgggcca ggaaatcaca tcctacactg cccaggagcc agacacattt atggaacaga       180
aaataacata tcggatttgg agagacactg ccaactggct ggagattaat ccggacactg       240
gtgccatttc c                                                            251

        <210> 346
        <211> 282
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(282)
        <223> n = A,T,C or G

    <400> 346
cgcgtctctg acactgtgat catgacaggg gttcaaacag aaagtgcctg ggccctcctt        60
ctaagtcttg ttaccaaaaa aaggaaaaag aaaagatctt ctcagttaca aattctggga       120
agggagacta tacctggctc ttgccctaag tgagaggtct tccctcccgc accaaaaaat       180
agaaaggctt tctatttcac tggcccaggt aggggaagg agagtaactt tgagtctgtg       240
ggtctcattt cccaaggtgc cttcaatgct catnaaaacc aa                          282

        <210> 347
        <211> 201
        <212> DNA
        <213> Homo sapien

        <220>
        <221> misc_feature
        <222> (1)...(201)
        <223> n = A,T,C or G

        <400> 347
acacacataa tattataaaa tgccatctaa ttggaaggag ctttctatca ttgcaagtca        60
taaatataac ttttaaaana ntactancag cttttaccta ngctcctaaa tgcttgtaaa       120
tctgagactg actggaccca cccagaccca gggcaaagat acatgttacc atatcatctt       180
tataaagaat tttttttgt c                                                  201

        <210> 348
        <211> 251
        <212> DNA
        <213> Homo sapien

        <400> 348
ctgttaatca caacatttgt gcatcacttg tgccaagtga gaaaatgttc taaaatcaca        60
agagagaaca gtgccagaat gaaactgacc ctaagtccca ggtgcccctg ggcaggcaga       120
aggagacact cccagcatgg aggagggttt atcttttcat cctaggtcag gtctacaatg       180
ggggaaggtt ttattataga actcccaaca gcccacctca ctcctgccac ccacccgatg       240
gccctgcctc c                                                            251

        <210> 349
        <211> 251
        <212> DNA
```

```
        <213> Homo sapien

        <400> 349
taaaaatcaa gccatttaat tgtatctttg aaggtaaaca atatatggga gctggatcac      60
aacccctgag gatgccagag ctatgggtcc agaacatggt gtggtattat caacagagtt     120
cagaagggtc tgaactctac gtgttaccag agaacataat gcaattcatg cattccactt     180
agcaattttg taaaatacca gaaacagacc ccaagagtct ttcaagatga ggaaaattca     240
actcctggtt t                                                          251


        <210> 350
        <211> 908
        <212> DNA
        <213> Homo sapien

        <400> 350
ctggacactt tgcgagggct tttgctggct gctgctgctg cccgtcatgc tactcatcgt      60
agcccgcccg gtgaagctcg ctgctttccc tacctcctta agtgactgcc aaacgcccac     120
cggctggaat tgctctggtt atgatgacag agaaatgat ctcttcctct gtgacaccaa      180
cacctgtaaa tttgatgggg aatgtttaag aattggagac actgtgactt gcgtctgtca     240
gttcaagtgc aacaatgact atgtgcctgt gtgtggctcc aatggggaga gctaccagaa     300
tgagtgttac ctgcgacagg ctgcatgcaa acagcagagt gagatacttg tggtgtcaga     360
aggatcatgt gccacagtcc atgaaggctc tggagaaact agtcaaaagg agacatccac     420
ctgtgatatt tgccagtttg gtgcagaatg tgacgaagat gccgaggatg tctggtgtgt     480
gtgtaatatt gactgttctc aaaccaactt caatccctc tgcgcttctg atgggaaatc      540
ttatgataat gcatgccaaa tcaaagaagc atcgtgtcag aaacaggaga aaattgaagt     600
catgtctttg ggtcgatgtc aagataacac aactacaact actaagtctg aagatgggca     660
ttatgcaaga acagattatg cagagaatgc taacaaatta gaagaaagtg ccagagaaca     720
ccacatacct tgtccggaac attacaatgg cttctgcatg catgggaagt gtgagcattc     780
tatcaatatg caggagccat cttgcaggtg tgatgctggt tatactggac aacactgtga     840
aaaaaaggac tacagtgttc tatacgttgt tcccggtcct gtacgatttc agtatgtctt     900
aatcgcag                                                             908


        <210> 351
        <211> 472
        <212> DNA
        <213> Homo sapien

        <400> 351
ccagttattt gcaagtggta agagcctatt taccataaat aatactaaga accaactcaa      60
gtcaaacctt aatgccattg ttattgtgaa ttaggattaa gtagtaattt tcaaaattca     120
cattaacttg attttaaaat cagwtttgyg agtcatttac cacaagctaa atgtgtacac     180
tatgataaaa acaaccattg tattcctgtt tttctaaaca gtcctaattt ctaacactgt     240
atatatcctt cgacatcaat gaactttgtt ttcttttact ccagtaataa agtaggcaca     300
gatctgtcca caacaaactt gccctctcat gccttgcctc tcaccatgct ctgctccagg     360
tcagcccccct tttggcctgt ttgttttgtc aaaaacctaa tctgcttctt gcttttcttg     420
gtaatatata tttagggaag atgttgcttt gcccacacac gaagcaaagt aa            472


        <210> 352
        <211> 251
        <212> DNA
        <213> Homo sapien

        <400> 352
ctcaaagcta atctctcggg aatcaaacca gaaaagggca aggatcttag gcatggtgga      60
tgtggataag gccaggtcaa tggctgcaag catgcagaga aagaggtaca tcggagcgtg     120
caggctgcgt tccgtcctta cgatgaagac cacgatgcag tttccaaaca ttgccactac     180
atacatggaa aggaggggga agccaaccca gaaatgggct ttctctaatc ctgggatacc     240
aataagcaca a                                                          251
```

```
<210> 353
<211> 436
<212> DNA
<213> Homo sapien

<400> 353
tttttttttt tttttttttt tttttacaa caatgcagtc atttatttat tgagtatgtg        60
cacattatgg tattattact atactgatta tatttatcat gtgacttcta attaraaaat       120
gtatccaaaa gcaaacagc agatatacaa aattaaagag acagaagata gacattaaca        180
gataaggcaa cttatacatt gacaatccaa atccaataca tttaaacatt tgggaaatga       240
gggggacaaa tggaagccar atcaaatttg tgtaaaacta ttcagtatgt ttcccttgct       300
tcatgtctga raaggctctc ccttcaatgg ggatgacaaa ctccaaatgc cacacaaatg       360
ttaacagaat actagattca cactggaacg ggggtaaaga agaaattatt ttctataaaa       420
gggctcctaa tgtagt                                                       436

<210> 354
<211> 854
<212> DNA
<213> Homo sapien

<400> 354
ccttttctag ttcaccagtt ttctgcaagg atgctggtta gggagtgtct gcaggaggag        60
caagtctgaa accaaatcta ggaaacatag gaaacgagcc aggcacaggg ctggtgggcc       120
atcagggacc accctttggg ttgatatttt gcttaatctg catcttttga gtaagatcat       180
ctggcagtag aagctgttct ccaggtacat ttctctagct catgtacaaa aacatcctga       240
aggactttgt caggtgcctt gctaaaagcc agatgcgttc ggcacttcct tggtctgagg       300
ttaattgcac acctacaggc actgggctca tgctttcaag tattttgtcc tcactttagg       360
gtgagtgaaa gatccccatt ataggagcac ttgggagaga tcatataaaa gctgactctt       420
gagtacatgc agtaatgggg tagatgtgtg tggtgtgtct tcattcctgc aagggtgctt       480
gttagggagt gtttccagga ggaacaagtc tgaaaccaat catgaaataa atggtaggtg       540
tgaactggaa aactaattca aaagagagat cgtgatatca gtgtggttga tacaccttgg       600
caatatggaa ggctctaatt tgcccatatt tgaaataata attcagcttt ttgtaataca       660
aaataacaaa ggattgagaa tcatggtgtc taatgtataa aagacccagg aaacataaat       720
atatcaactg cataaatgta aaatgcatgt gacccaagaa ggccccaaag tggcagacaa       780
cattgtaccc attttccctt ccaaaatgtg agcggcgggc ctgctgcttt caaggctgtc       840
acacgggatg tcag                                                        854

<210> 355
<211> 676
<212> DNA
<213> Homo sapien

<400> 355
gaaattaagt atgagctaaa ttccctgtta aaacctctag gggtgacaga tctcttcaac        60
caggtcaaag ctgatctttc tggaatgtca ccaaccaagg gcctatattt atcaaaagcc       120
atccacaagt catacctgga tgtcagcgaa gagggcacgg aggcagcagc agccactggg       180
gacagcatcg ctgtaaaaag cctaccaatg agagctcagt tcaaggcgaa ccacccttc        240
ctgttcttta taaggcacac tcataccaac acgatcctat tctgtggcaa gcttgcctct       300
ccctaatcag atggggttga gtaaggctca gagttgcaga tgaggtgcag agacaatcct       360
gtgactttcc cacggccaaa aagctgttca cacctcacgc acctctgtgc ctcagttgc        420
tcatctgcaa aataggtcta ggatttcttc caaccatttc atgagttgtg aagctaaggc       480
tttgttaatc atggaaaaag gtagacttat gcagaaagcc tttctggctt tcttatctgt       540
ggtgtctcat ttgagtgctg tccagtgaca tgatcaagtc aatgagtaaa attttaaggg       600
attagatttt cttgacttgt atgtatctgt gagatcttga ataagtgacc tgacatctct       660
gcttaaagaa aaccag                                                       676

<210> 356
```

```
        <211> 574
        <212> DNA
        <213> Homo sapien

        <400> 356
ttttttttttt tttttcagga aaacattctc ttactttatt tgcatctcag caaaggttct        60
catgtggcac ctgactggca tcaaaccaaa gttcgtaggc caacaaagat gggccactca       120
caagcttccc atttgtagat ctcagtgcct atgagtatct gacacctgtt cctctcttca       180
gtctcttagg gaggcttaaa tctgtctcag gtgtgctaag agtgccagcc caaggkggtc       240
aaaagtccac aaaactgcag tctttgctgg gatagtaagc caagcagtgc ctggacagca       300
gagttctttt cttgggcaac agataaccag acaggactct aatcgtgctc ttattcaaca       360
ttcttctgtc tctgcctaga ctggaataaa aagccaatct ctctcgtggc acagggaagg       420
agatacaagc tcgtttacat gtgatagatc taacaaaggc atctaccgaa gtctggtctg       480
gatagacggc acagggagct cttaggtcag cgctgctggt tggaggacat tcctgagtcc       540
agctttgcag cctttgtgca acagtacttt ccca                                   574

        <210> 357
        <211> 393
        <212> DNA
        <213> Homo sapien

        <400> 357
ttttttttttt ttttttttttt ttttttttttt tacagaatat aratgcttta tcactgkact        60
taatatggkg kcttgttcac tatacttaaa aatgcaccac tcataaatat ttaattcagc       120
aagccacaac caaracttga ttttatcaac aaaaacccct aaatataaac ggsaaaaaag       180
atagatataa ttattccagt ttttttaaaa cttaaaaarat attccattgc cgaattaara       240
araarataag tgttatatgg aaagaagggc attcaagcac actaaaraaa cctgaggkaa       300
gcataatctg tacaaaatta aactgtcctt tttggcattt taacaaattt gcaacgktct       360
tttttttctt tttctgtttt ttttttttttt tac                                   393

        <210> 358
        <211> 630
        <212> DNA
        <213> Homo sapien

        <400> 358
acagggtaaa caggaggatc cttgctctca cggagcttac attctagcag gaggacaata        60
ttaatgttta taggaaaatg atgagtttat gacaaaggaa gtagatagtg ttttacaaga       120
gcatagagta gggaagctaa tccagcacag ggaggtcaca gagacatccc taaggaagtg       180
gagtttaaac tgagagaagc aagtgcttaa actgaaggat gtgttgaaga agaagggaga       240
gtagaacaat ttgggcagag ggaaccttat agaccctaag gtgggaaggt tcaaagaact       300
gaaagagagc tagaacagct ggagccgttc tccggtgtaa agaggagtca aagagataag       360
attaaagatg tgaagattaa gatcttggtg gcattcaggg attggcactt ctacaagaaa       420
tcactgaagg gagtaatgtg acattacttt tcacttcagg atggccattc taactccagg       480
gggtagactg gactaggtaa gactggaggc aggtagacct cttctaaggc ctgcgatagt       540
gaaagacaaa aataagtggg gaaattcagg ggatagtgaa aatcagtagg acttaatgag       600
caagccagag gttcctccac aacaaccagt                                        630

        <210> 359
        <211> 620
        <212> DNA
        <213> Homo sapien

        <400> 359
acagcattcc aaaatataca tctagagact aarrgtaaat gctctatagt gaagaagtaa        60
taattaaaaa atgctactaa tatagaaaat ttataatcag aaaaataaat attcagggag       120
ctcaccagaa gaataaagtg ctctgccagt tattaaagga ttactgctgg tgaattaaat       180
atggcattcc ccaagggaaa tagagagatt cttctggatt atgttcaata tttatttcac       240
```

```
aggattaact gttttaggaa cagatataaa gcttcgccac ggaagagatg gacaaagcac      300
aaagacaaca tgatacctta ggaagcaaca ctaccctttc aggcataaaa tttggagaaa      360
tgcaacatta tgcttcatga ataatatgta gaaagaaggt ctgatgaaaa tgacatcctt      420
aatgtaagat aactttataa gaattctggg tcaaataaaa ttctttgaag aaaacatcca      480
aatgtcattg acttatcaaa tactatcttg gcatataacc tatgaaggca aaactaaaca      540
aacaaaaagc tcacaccaaa caaaaccatc aacttatttt gtattctata acatacgaga      600
ctgtaaagat gtgacagtgt                                                  620
```

          <210> 360
          <211> 431
          <212> DNA
          <213> Homo sapien

          <400> 360
```
aaaaaaaaaa agccagaaca acatgtgata gataaatatga ttggctgcac acttccagac      60
tgatgaatga tgaacgtgat ggactattgt atggagcaca tcttcagcaa gagggggaaa      120
tactcatcat ttttggccag cagttgtttg atcaccaaac atcatgccag aatactcagc      180
aaaccttctt agctcttgag aagtcaaagt ccggggggaat ttattcctgg caattttaat      240
tggactcctt atgtgagagc agcggctacc cagctggggt ggtggagcga acccgtcact      300
agtggacatg cagtggcaga gctcctggta accacctaga ggaatacaca ggcacatgtg      360
tgatgccaag cgtgacacct gtagcactca aatttgtctt gttttttgtct ttcggtgtgt      420
agattcttag t                                                          431
```

          <210> 361
          <211> 351
          <212> DNA
          <213> Homo sapien

          <400> 361
```
acactgattt ccgatcaaaa gaatcatcat ctttaccttg acttttcagg gaattactga      60
actttcttct cagaagatag ggcacagcca ttgccttggc ctcacttgaa gggtctgcat      120
ttgggtcctc tggtctcttg ccaagtttcc cagccactcg agggagaaat atcgggaggt      180
ttgacttcct ccggggcttt cccgagggct tcaccgtgag ccctgcggcc ctcagggctg      240
caatcctgga ttcaatgtct gaaacctcgc tctctgcctg ctggacttct gaggccgtca      300
ctgccactct gtcctccagc tctgacagct cctcatctgt ggtcctgttg t              351
```

          <210> 362
          <211> 463
          <212> DNA
          <213> Homo sapien

          <400> 362
```
acttcatcag gccataatgg gtgcctcccg tgagaatcca agcacctttg gactgcgcga      60
tgtagatgag ccggctgaag atcttgcgca tgcgcggctt cagggcgaag ttcttggcgc      120
ccccggtcac agaaatgacc aggttgggtg ttttcaggtg ccagtgctgg gtcagcagct      180
cgtaaaggat ttccgcgtcc gtgtcgcagg acagacgtat atacttccct ttcttcccca      240
gtgtctcaaa ctgaatatcc ccaaaggcgt cggtaggaaa ttccttggtg tgtttcttgt      300
agttccattt ctcactttgg ttgatctggg tgccttccat gtgctggctc tgggcatagc      360
cacacttgca cacattctcc ctgataagca cgatggtgtg gacaggaagg aaggatttca      420
ttgagcctgc ttatggaaac tggtattgtt agcttaaata gac                       463
```

          <210> 363
          <211> 653
          <212> DNA
          <213> Homo sapien

          <220>
          <221> misc_feature

```
       <222> (1)...(653)
       <223> n = A,T,C or G

       <400> 363
acccccgagt ncctgnctgg catactgnga acgaccaacg acacacccaa gctcggcctc      60
ctcttggnga ttctgggtga catcttcatg aatggcaacc gtgccagwga ggctgtcctc     120
tgggaggcac tacgcaagat gggactgcgt cctggggtga gacatcctct ccttggagat     180
ctaacgaaac ttctcaccta tgagttgtaa agcagaaata cctgnactac agacgagtgc     240
ccaacagcaa cccccggaa gtatgagttc ctctrgggcc tccgttccta ccatgagasc      300
tagcaagatg naagtgttga gantcattgc agaggttcag aaaagagacc cntcgtgact     360
ggtctgcaca gttcatggag gctgcagatg aggccttgga tgctctggat gctgctgcag     420
ctgaggccga agcccgggct gaagcaagaa cccgcatggg aattggagat gaggctgtgt     480
ntgggccctg gagctgggat gacattgagt ttgagctgct gacctgggat gaggaaggag     540
attttggaga tccntggtcc agaattccat ttaccttctg ggccagatac caccagaatg     600
cccgctccag attccctcag acctttgccg gtcccattat tggtcstggt ggt           653

       <210> 364
       <211> 401
       <212> DNA
       <213> Homo sapien

       <400> 364
actagaggaa agacgttaaa ccactctact accacttgtg gaactctcaa agggtaaatg      60
acaaagccaa tgaatgactc taaaaacaat atttacattt aatggtttgt agacaataaa     120
aaaacaaggt ggatagatct agaattgtaa cattttaaga aaaccatagc atttgacaga     180
tgagaaagct caattataga tgcaaagtta taactaaact actatagtag taaagaaata     240
catttcacac ccttcatata aattcactat cttggcttga ggcactccat aaaatgtatc     300
acgtgcatag taaatcttta tatttgctat ggcgttgcac tagaggactt ggactgcaac     360
aagtggatgc gcggaaaatg aaatcttctt caatagccca g                        401

       <210> 365
       <211> 356
       <212> DNA
       <213> Homo sapien

       <400> 365
ccagtgtcat atttgggctt aaaatttcaa gaagggcact tcaaatggct ttgcatttgc      60
atgtttcagt gctagagcgt aggaatagac cctggcgtcc actgtgagat gttcttcagc     120
taccagagca tcaagtctct gcagcaggtc attcttgggt aaagaaatga cttccacaaa     180
ctctccatcc cctggctttg gcttcggcct tgcgttttcg gcatcatctc cgttaatggt     240
gactgtcacg atgtgtatag tacagtttga caagcctggg tccatacaga ccgctggaga     300
acattcggca atgtcccctt tgtagccagt ttcttcttcg agctcccgga gagcag         356

       <210> 366
       <211> 1851
       <212> DNA
       <213> Homo sapien

       <400> 366
tcatcaccat tgccagcagc ggcaccgtta gtcaggtttt ctgggaatcc cacatgagta      60
cttccgtgtt cttcattctt cttcaatagc cataaatctt ctagctctgg ctggctgttt     120
tcacttcctt taagcctttg tgactcttcc tctgatgtca gctttaagtc ttgttctgga     180
ttgctgtttt cagaagagat ttttaacatc tgttttttctt tgtagtcaga aagtaactgg     240
caaattacat gatgatgact agaaacagca tactctctgg ccgtctttcc agatcttgag     300
aagatacatc aacattttgc tcaagtagag ggctgactat acttgctgat ccacaacata     360
cagcaagtat gagagcagtt cttccatatc tatccagcgc atttaaattc gctttttttct     420
tgattaaaaa tttcaccact tgctgttttt gctcatgtat accaagtagc agtggtgtga     480
ggccatgctt gttttttgat tcgatatcag caccgtataa gagcagtgct ttggccatta     540
```

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atttatcttc attgtagaca gcatagtgta gagtggtatt tccatactca tctggaatat    600
ttggatcagt gccatgttcc agcaacatta acgcacattc atcttcctgg cattgtacgg    660
cctttgtcag agctgtcctc tttttgttgt caaggacatt aagttgacat cgtctgtcca    720
gcacgagttt tactacttct gaattcccat tggcagaggc cagatgtaga gcagtcctct    780
tttgcttgtc cctcttgttc acatccgtgt ccctgagcat gacgatgaga tcctttctgg    840
ggactttacc ccaccaggca gctctgtgga gcttgtccag atcttctcca tggacgtggt    900
acctgggatc catgaaggcg ctgtcatcgt agtctcccca agcgaccacg ttgctcttgc    960
cgctcccctg cagcagggga agcagtggca gcaccacttg cacctcttgc tcccaagcgt   1020
cttcacagag gagtcgttgt ggtctccaga agtgcccacg ttgctcttgc cgctccccct   1080
gtccatccag ggaggaagaa atgcaggaaa tgaaagatgc atgcacgatg gtatactcct   1140
cagccatcaa acttctggac agcaggtcac ttccagcaag gtggagaaag ctgtccaccc   1200
acagaggatg agatccagaa accacaatat ccattcacaa acaaacactt ttcagccaga   1260
cacaggtact gaaatcatgt catctgcggc aacatggtgg aacctaccca atcacacatc   1320
aagagatgaa gacactgcag tatatctgca caacgtaata ctcttcatcc ataacaaaat   1380
aatataattt tcctctggag ccatatggat gaactatgaa ggaagaactc cccgaagaag   1440
ccagtcgcag agaagccaca ctgaagctct gtcctcagcc atcagcgcca cggacaggar   1500
tgtgtttctt ccccagtgat gcagcctcaa gttatcccga agctgccgca gcacacggtg   1560
gctcctgaga aacaccccag ctcttccggt ctaacacagg caagtcaata aatgtgataa   1620
tcacataaac agaattaaaa gcaaagtcac ataagcatct caacagacac agaaaaggca   1680
tttgacaaaa tccagcatcc ttgtatttat tgttgcagtt ctcagaggaa atgcttctaa   1740
cttttcccca tttagtatta tgttggctgt gggcttgtca taggtggttt ttattactttt  1800
aaggtatgtc ccttctatgc ctgtttttgct gagggttttta attctcgtgc c          1851
```

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        <210> 367
        <211> 668
        <212> DNA
        <213> Homo sapien


        <400> 367
cttgagcttc caaataygga agactggccc ttacacasgt caatgttaaa atgaatgcat     60
ttcagtattt tgaagataaa attrgtagat ctataccttg ttttttgatt cgatatcagc    120
accrtataag agcagtgctt tggccattaa tttatctttc attrtagaca gcrtagtgya    180
gagtggtatt tccatactca tctggaatat ttggatcagt gccatgttcc agcaacatta    240
acgcacattc atcttcctgg cattgtacgg cctgtcagta ttagacccaa aaacaaatta    300
catatcttag gaattcaaaa taacattcca cagctttcac caactagtta tatttaaagg    360
agaaaactca tttttatgcc atgtattgaa atcaaaccca cctcatgctg atatagttgg    420
ctactgcata cctttatcag agctgtcctc tttttgttgt caaggacatt aagttgacat    480
cgtctgtcca gcaggagttt tactacttct gaattcccat tggcagaggc cagatgtaga    540
gcagtcctat gagagtgaga agactttta ggaaattgta gtgcactagc tacagccata    600
gcaatgattc atgtaactgc aaacactgaa tagcctgcta ttactctgcc ttcaaaaaaa    660
aaaaaaaa                                                              668
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        <211> 1512
        <212> DNA
        <213> Homo sapien


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tgggctgggc trgaatcccc tgctgggggtt ggcaggtttt ggctgggatt gactttttytc   120
ttcaaacaga ttggaaaccc ggagttacct gctagttggt gaaactggtt ggtagacgcg    180
atctgttggc tactactggc ttctcctggc tgttaaaagc agatggtggt tgaggttgat    240
tccatgccgg ctgcttcttc tgtgaagaag ccatttggtc tcaggagcaa gatgggcaag    300
tggtgctgcc gttgcttccc ctgctgcagg gagagcggca agagcaacgt gggcacttct    360
ggagaccacg acgactctgc tatgaagaca ctcaggagca agatgggcaa gtggtgccgc    420
cactgcttcc cctgctgcag ggggagtggc aagagcaacg tgggcgcttc tggagaccac    480
gacgaytctg ctatgaagac actcaggaac aagatgggca agtggtgctg ccactgcttc    540
ccctgctgca gggggagcrg caagagcaag gtgggcgctt ggggagacta cgatgacagt    600
```

```
gccttcatgg agcccaggta ccacgtccgt ggagaagatc tggacaagct ccacagagct      660
gcctggtggg gtaaagtccc cagaaaggat ctcatcgtca tgctcaggga cactgacgtg      720
aacaagaagg acaagcaaaa gaggactgct ctacatctgg cctctgccaa tgggaattca      780
gaagtagtaa aactcstgct ggacagacga tgtcaactta atgtccttga caacaaaaag      840
aggacagctc tgayaaaggc cgtacaatgc caggaagatg aatgtgcgtt aatgttgctg      900
gaacatggca ctgatccaaa tattccagat gagtatggaa ataccactct rcactaygct      960
rtctayaatg aagataaatt aatggccaaa gcactgctct tatayggtgc tgatatcgaa     1020
tcaaaaaaca aggtatagat ctactaattt tatcttcaaa atactgaaat gcattcattt     1080
taacattgac gtgtgtaagg gccagtcttc cgtatttgga agctcaagca taacttgaat     1140
gaaaatattt tgaaatgacc taattatctm agactttatt ttaaatattg ttattttcaa     1200
agaagcatta gagggtacag ttttttttttt ttaaatgcac ttctggtaaa tacttttgtt     1260
gaaaacactg aatttgtaaa aggtaatact tactattttt caattttttcc ctcctaggat     1320
tttttttcccc taatgaatgt aagatggcaa aatttgccct gaaataggtt ttacatgaaa     1380
actccaagaa aagttaaaca tgtttcagtg aatagagatc ctgctccttt ggcaagttcc     1440
taaaaaacag taatagatac gaggtgatgc gcctgtcagt ggcaaggttt aagatatttc     1500
tgatctcgtg cc                                                         1512
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    <210>  369
    <211>  1853
    <212>  DNA
    <213>  Homo sapien

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ttcaaacaga ttggaaaccc ggagttacct gctagttggt gaaactggtt ggtagacgcg     180
atctgttggc tactactggc ttctcctggc tgttaaaagc agatggtggt tgaggttgat     240
tccatgccgg ctgcttcttc tgtgaagaag ccatttggtc tcaggagcaa gatgggcaag     300
tggtgctgcc gttgcttccc ctgctgcagg gagagcggca agagcaacgt gggcacttct     360
ggagaccacg acgactctgc tatgaagaca ctcaggagca agatgggcaa gtggtgccgc     420
cactgcttcc cctgctgcag ggggagtggc aagagcaacg tgggcgcttc tggagaccac     480
gacgaytctg ctatgaagac actcaggaac aagatgggca agtggtgctg ccactgcttc     540
ccctgctgca ggggggagcrg caagagcaag gtgggcgctt ggggagacta cgatgacagy     600
gccttcatgg akcccaggta ccacgtccrt ggagaagatc tggacaagct ccacagagct      660
gcctggtggg gtaaagtccc cagaaaggat ctcatcgtca tgctcaggga cackgaygtg      720
aacaagargg acaagcaaaa gaggactgct ctacatctgg cctctgccaa tgggaattca      780
gaagtagtaa aactcstgct ggacagacga tgtcaactta atgtccttga caacaaaaag      840
aggacagctc tgayaaaggc cgtacaatgc caggaagatg aatgtgcgtt aatgttgctg      900
gaacatggca ctgatccaaa tattccagat gagtatggaa ataccactct rcactaygct      960
rtctayaatg aagataaatt aatggccaaa gcactgctct tatayggtgc tgatatcgaa     1020
tcaaaaaaca agcatggcct cacaccactg ytacttggtr tacatgagca aaaacagcaa     1080
gtsgtgaaat ttttaatyaa gaaaaaagcg aatttaaaat gcrctggata gatatggaag     1140
ractgctctc atacttgctg tatgttgtgg atcagcaagt atagtcagcc ytctacttga     1200
gcaaaatrtt gatgtatctt ctcaagatct ggaaagacgg ccagagagta tgctgtttct     1260
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caaaggctta aaggaagtga aaacagccag ccagaggcat ggaaactttt aaatttaaac     1440
ttttggttta atgtttttttt tttttgcctt aataatatta gatagtccca aatgaaatwa     1500
cctatgagac taggctttga gaatcaatag attctttttt taagaatctt ttggctagga     1560
gcggtgtctc acgcctgtaa ttccagcacc ttgagaggct gaggtgggca gatcacgaga     1620
tcaggagatc gagaccatcc tggctaacac ggtgaaaccc catctctact aaaaatacaa     1680
aaacttagct gggtgtggtg gcgggtgcct gtagtcccag ctactcagga rgctgaggca     1740
ggagaatggc atgaacccgg gaggtggagg ttgcagtgag ccgagatccg ccactacact     1800
ccagcctggg tgacagagca agactctgtc tcaaaaaaaa aaaaaaaaa aaa            1853
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    <210>  370
    <211>  2184
    <212>  DNA
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<213> Homo sapien

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tttcctctga gaactgcaac aataaataca aggatgctgg attttgtcaa atgccttttc     180
tgtgtctgtt gagatgctta tgtgactttg cttttaattc tgtttatgtg attatcacat     240
ttattgactt gcctgtgtta gaccggaaga gctggggtgt ttctcaggag ccaccgtgtg     300
ctgcggcagc ttcgggataa cttgaggctg catcactggg gaagaaacac aytcctgtcc     360
gtggcgctga tggctgagga cagagcttca gtgtggcttc tctgcgactg gcttcttcgg     420
ggagttcttc cttcatagtt catccatatg gctccagagg aaaattatat tattttgtta     480
tggatgaaga gtattacgtt gtgcagatat actgcagtgt cttcatctct tgatgtgtga     540
ttgggtaggt tccaccatgt tgccgcagat gacatgattt cagtacctgt gtctggctga     600
aaagtgtttg tttgtgaatg gatattgtgg tttctggatc tcatcctctg tgggtggaca     660
gctttctcca ccttgctgga agtgacctgc tgtccagaag tttgatggct gaggagtata     720
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cgaatttaaa tgcgctggat agatatggaa gaactgctct catacttgct gtatgttgtg    1500
gatcagcaag tatagtcagc cctctacttg agcaaaatgt tgatgtatct tctcaagatc    1560
tggaaagacg gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact    1620
ttctgactac aaagaaaaac agatgttaaa aatctcttct gaaaacagca atccagaaca    1680
agacttaaag ctgacatcag aggaagagtc acaaaggctt aaaggaagtg aaaacagcca    1740
gccagaggca tggaaacttt taaatttaaa cttttggttt aatgtttttt ttttttgcct    1800
taataatatt agatagtccc aaatgaaatw acctatgaga ctaggctttg agaatcaata    1860
gattctttt ttaagaatct tttggctagg agcggtgtct cacgcctgta attccagcac    1920
cttgagaggc tgaggtgggc agatcacgag atcaggagat cgagaccatc ctggctaaca    1980
cggtgaaacc ccatctctac taaaaataca aaaacttagc tgggtgtggt ggcgggtgcc    2040
tgtagtccca gctactcagg argctgaggc aggagaatgg catgaacccg ggaggtggag    2100
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ctcaaaaaaa aaaaaaaaa aaaa                                            2184

    <210> 371
    <211> 1855
    <212> DNA
    <213> Homo sapien

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    <223> n = A,T,C or G

    <400> 371
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gccgcccccg cataaccgtc agactggcct gtaacggctt gcaggcgcac gccgcacgcg     180
cgtaacggct tggctgccct gtaacggctt gcacgtgcat gctgcacgcg cgttaacggc     240
ttggctggca tgtagccgct tggcttggct ttgcattytt tgctkggctk ggcgttgkty     300
tcttggattg acgcttcctc cttggatkga cgtttcctcc ttggatkgac gtttcytyty     360
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gggcgtgggc  tttccccggg  tgggtgtggg  ttttcctggg  gtggggtggg  ctgtgctggg      540
atcccctgc   tggggttggc  agggattgac  tttttcttc   aaacagattg  gaaacccgga      600
gtaacntgct  agttggtgaa  actggttggt  agacgcgatc  tgctggtact  actgtttctc      660
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agaagccatt  tggtctcagg  agcaagatgg  gcaagtggtg  cgccactgct  tccctgctg       780
caggggagc   ggcaagagca  acgtgggcac  ttctggagac  cacaacgact  cctctgtgaa      840
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gtaccacgtc  crtggagaag  atctggacaa  gctccacaga  gctgcctggt  ggggtaaagt     1020
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ggccgtacaa  tgccaggaag  atgaatgtgc  gttaatgttg  ctggaacatg  gcactgatcc     1260
aaatattcca  gatgagtatg  gaaataccac  tctacactat  gctgtctaca  atgaagataa     1320
attaatggcc  aaagcactgc  tcttatacgg  tgctgatatc  gaatcaaaaa  acaaggtata     1380
gatctactaa  ttttatcttc  aaaatactga  aatgcattca  ttttaacatt  gacgtgtgta     1440
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        <211>  1059
        <212>  DNA
        <213>  Homo sapien

        <400>  372
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gcgcttgrgg  agactmcgat  gacagygcct  tcatggagcc  caggtaccac  gtccgtggag      180
aagatctgga  caagctccac  agagctgccc  tggtggggta  aagtccccag  aaaggatctc      240
atcgtcatgc  tcagggacac  tgaygtgaac  aagarggaca  agcaaaagag  gactgctcta      300
catctggcct  ctgccaatgg  gaattcagaa  gtagtaaaac  tcstgctgga  cagacgatgt      360
caacttaatg  tccttgacaa  caaaaagagg  acagctctga  yaaaggccgt  acaatgccag      420
gaagatgaat  gtgcgttaat  gttgctggaa  catggcactg  atccaaatat  tccagatgag      480
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ttgccctgaa  ataggtttta  catgaaaact  ccaagaaaag  ttaaacatgt  ttcagtgaat      960
agagatcctg  ctcctttggc  aagttcctaa  aaaacagtaa  tagatacgag  gtgatgcgcc     1020
tgtcagtggc  aaggtttaag  atatttctga  tctcgtgcc                              1059
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        <210>  373
        <211>  1155
        <212>  DNA
        <213>  Homo sapien

        <400>  373
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aggagcaaga tgggcaagtg gtgctgccgt tgcttcccct gctgcaggga gagcggcaag      120
agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag      180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg      240
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ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata      960
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg     1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac     1080
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaaa tgtctcaaga     1140
accagaaata aataa                                                      1155
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<210> 374
<211> 2000
<212> DNA
<213> Homo sapien

<400> 374
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agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag      180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg      240
ggcgcttctg gagaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag      300
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gacaagctcc acagagctgc ctggtggggt aaagtcccca gaaaggatct catcgtcatg      480
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc      540
tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat      600
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa      660
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accactctgc actacgctat ctataatgaa gataaattaa tggccaaagc actgctctta      780
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta      840
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gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg     1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac     1080
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cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa     1440
aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca     1500
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tttatggcta tcgaagaaat gaagaagcac ggaagtactc atgtcggatt cccagaaaac     1620
ctgactaatg gtgccactgc tggcaatggt gatgatggat taattcctcc aaggaagagc     1680
agaacacctg aaagccagca atttcctgac actgagaatg aagagtatca cagtgacgaa     1740
caaaatgata ctcagaagca attttgtgaa gaacagaaca ctggaatatt acacgatgag     1800
attctgattc atgaagaaaa gcagatagaa gtggttgaaa aaatgaattc tgagctttct     1860
cttagttgta agaaagaaaa agacatcttg catgaaaata gtacgttgcg ggaagaaatt     1920
```

```
gccatgctaa gactggagct agacacaatg aaacatcaga gccagctaaa aaaaaaaaaa      1980
aaaaaaaaaa aaaaaaaaaa                                                  2000
```

```
<210> 375
<211> 2040
<212> DNA
<213> Homo sapien
```

```
<400> 375
atggtggttg aggttgattc catgccggct gcctcttctg tgaagaagcc atttggtctc       60
aggagcaaga tgggcaagtg gtgctgccgt tgcttcccct gctgcaggga gagcggcaag      120
agcaacgtgg gcacttctgg agaccacgac gactctgcta tgaagacact caggagcaag      180
atgggcaagt ggtgccgcca ctgcttcccc tgctgcaggg ggagtggcaa gagcaacgtg      240
ggcgcttctg agaccacga cgactctgct atgaagacac tcaggaacaa gatgggcaag       300
tggtgctgcc actgcttccc ctgctgcagg gggagcggca agagcaaggt gggcgcttgg      360
ggagactacg atgacagtgc cttcatggag cccaggtacc acgtccgtgg agaagatctg      420
gacaagctcc acagagctgc ctggtggggt aaagtcccca gaaaggatct catcgtcatg      480
ctcagggaca ctgacgtgaa caagaaggac aagcaaaaga ggactgctct acatctggcc      540
tctgccaatg ggaattcaga agtagtaaaa ctcctgctgg acagacgatg tcaacttaat      600
gtccttgaca acaaaaagag gacagctctg ataaaggccg tacaatgcca ggaagatgaa      660
tgtgcgttaa tgttgctgga acatggcact gatccaaata ttccagatga gtatggaaat      720
accactctgc actacgctat ctataatgaa gataaattaa tggccaaagc actgctctta      780
tatggtgctg atatcgaatc aaaaaacaag catggcctca caccactgtt acttggtgta      840
catgagcaaa aacagcaagt cgtgaaattt ttaatcaaga aaaaagcgaa tttaaatgca      900
ctggatagat atggaaggac tgctctcata cttgctgtat gttgtggatc agcaagtata      960
gtcagccttc tacttgagca aaatattgat gtatcttctc aagatctatc tggacagacg     1020
gccagagagt atgctgtttc tagtcatcat catgtaattt gccagttact ttctgactac     1080
aaagaaaaac agatgctaaa aatctcttct gaaaacagca atccagaaca agacttaaag     1140
ctgacatcag aggaagagtc acaaaggttc aaaggcagtg aaaatagcca gccagagaaa     1200
atgtctcaag aaccagaaat aaataaggat ggtgatagag aggttgaaga agaaatgaag     1260
aagcatgaaa gtaataatgt gggattacta gaaaacctga ctaatggtgt cactgctggc     1320
aatggtgata atggattaat tcctcaaagg aagagcagaa cacctgaaaa tcagcaattt     1380
cctgacaacg aaagtgaaga gtatcacaga atttgcgaat tagtttctga ctacaaagaa     1440
aaacagatgc caaaatactc ttctgaaaac agcaacccag aacaagactt aaagctgaca     1500
tcagaggaag agtcacaaag gcttgagggc agtgaaaatg ccagccaga gaaaagatct      1560
caagaaccag aaataaataa ggatggtgat agagagctag aaaattttat ggctatcgaa     1620
gaaatgaaga agcacggaag tactcatgtc ggattcccag aaaacctgac taatggtgcc     1680
actgctggca atggtgatga tggattaatt cctccaagga gagcagaac acctgaaagc      1740
cagcaatttc ctgacactga gaatgaagag tatcacagtg acgaacaaaa tgatactcag     1800
aagcaatttt gtgaagaaca gaacactgga atattacacg atgagattct gattcatgaa     1860
gaaaagcaga tagaagtggt tgaaaaaatg aattctgagc tttctcttag ttgtaagaaa     1920
gaaaaagaca tcttgcatga aaatagtacg ttgcgggaag aaattgccat gctaagactg     1980
gagctagaca caatgaaaca tcagagccag ctaaaaaaaa aaaaaaaaaa aaaaaaaaaa     2040
```

```
<210> 376
<211> 329
<212> PRT
<213> Homo sapien
```

```
<400> 376
Met Asp Ile Val Val Ser Gly Ser His Pro Leu Trp Val Asp Ser Phe
1               5                   10                  15
Leu His Leu Ala Gly Ser Asp Leu Leu Ser Arg Ser Leu Met Ala Glu
            20                  25                  30
Glu Tyr Thr Ile Val His Ala Ser Phe Ile Ser Cys Ile Ser Ser Ser
        35                  40                  45
Leu Asp Gly Gln Gly Glu Arg Gln Glu Gln Arg Gly His Phe Trp Arg
    50                  55                  60
```

```
Pro Gln Arg Leu Leu Cys Glu Asp Ala Trp Glu Gln Glu Val Gln Val
65              70              75              80
Val Leu Pro Leu Leu Pro Leu Leu Gln Gly Ser Gly Lys Ser Asn Val
            85              90              95
Val Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr
            100             105             110
His Val His Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp
        115             120             125
Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp
    130             135             140
Val Asn Lys Arg Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser
145             150             155             160
Ala Asn Gly Asn Ser Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys
            165             170             175
Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala
            180             185             190
Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly
    195             200             205
Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr
    210             215             220
Ala Val Tyr Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr
225             230             235             240
Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu
            245             250             255
Leu Gly Ile His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys
            260             265             270
Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu
    275             280             285
Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu
    290             295             300
Glu Gln Asn Val Asp Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu
305             310             315             320
Ser Met Leu Phe Leu Val Ile Ile Met
            325
```

```
            <210>  377
            <211>  148
            <212>  PRT
            <213>  Homo sapien

            <220>
            <221>  VARIANT
            <222>  (1)...(148)
            <223>  Xaa = Any Amino Acid

            <400>  377
```

```
Met Thr Xaa Pro Ser Trp Ser Pro Gly Thr Thr Ser Val Glu Lys Ile
1               5               10              15
Trp Thr Ser Ser Thr Glu Leu Pro Trp Trp Gly Lys Val Pro Arg Lys
            20              25              30
Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Xaa Asp Lys
        35              40              45
Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu
    50              55              60
Val Val Lys Leu Xaa Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp
65              70              75              80
Asn Lys Lys Arg Thr Ala Leu Xaa Lys Ala Val Gln Cys Gln Glu Asp
                85              90              95
```

```
Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro
            100                 105                 110
Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Xaa Tyr Asn Glu Asp
            115                 120                 125
Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser
            130                 135                 140
Lys Asn Lys Val
145


        <210> 378
        <211> 1719
        <212> PRT
        <213> Homo sapien


        <400> 378
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1               5                   10                  15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
            20                  25                  30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
        35                  40                  45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
    50                  55                  60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65                  70                  75                  80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
            85                  90                  95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
            100                 105                 110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
            115                 120                 125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
            130                 135                 140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145                 150                 155                 160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
            165                 170                 175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
            180                 185                 190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
            195                 200                 205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
            210                 215                 220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225                 230                 235                 240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
            245                 250                 255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
            260                 265                 270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
            275                 280                 285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
            290                 295                 300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305                 310                 315                 320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
            325                 330                 335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
```

```
                    340                     345                  350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
            355                     360                  365
Ser Ser Glu Asn Ser Asn Pro Glu Asn Val Ser Arg Thr Arg Asn Lys
    370                     375                  380
Pro Arg Thr His Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser
385                     390                  395                  400
Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys
                405                     410                  415
Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly
                420                     425                  430
Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys
            435                     440                  445
Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly
            450                     455                  460
Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys
465                     470                  475                  480
Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys
                485                     490                  495
Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp
            500                     505                  510
Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu
            515                     520                  525
Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp
    530                     535                  540
Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln
545                     550                  555                  560
Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val
                565                     570                  575
Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn
            580                     585                  590
Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu
            595                     600                  605
Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp
    610                     615                  620
Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys
625                     630                  635                  640
Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys
                645                     650                  655
Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys
                660                     665                  670
Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala
            675                     680                  685
Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly
            690                     695                  700
Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser
705                     710                  715                  720
Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser
                725                     730                  735
His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln
            740                     745                  750
Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys
            755                     760                  765
Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser
    770                     775                  780
Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp
785                     790                  795                  800
Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly
```

```
                              805                      810                      815
            Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn
                        820                      825                      830
            Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe
                        835                      840                      845
            Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser
                        850                      855                      860
            Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn
            865                      870                      875                      880
            Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu
                        885                      890                      895
            Glu Gly Ser Glu Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile
                        900                      905                      910
            Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn
                        915                      920                      925
            Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro
                        930                      935                      940
            Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu
            945                      950                      955                      960
            Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe
                        965                      970                      975
            Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His
                        980                      985                      990
            Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser
                        995                      1000                     1005
            Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu
                        1010                     1015                     1020
            Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His
            1025                     1030                     1035                     1040
            Gln Ser Gln Leu Pro Arg Thr His Met Val Val Glu Val Asp Ser Met
                        1045                     1050                     1055
            Pro Ala Ala Ser Ser Val Lys Lys Pro Phe Gly Leu Arg Ser Lys Met
                        1060                     1065                     1070
            Gly Lys Trp Cys Cys Arg Cys Phe Pro Cys Cys Arg Glu Ser Gly Lys
                        1075                     1080                     1085
            Ser Asn Val Gly Thr Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr
                        1090                     1095                     1100
            Leu Arg Ser Lys Met Gly Lys Trp Cys Arg His Cys Phe Pro Cys Cys
            1105                     1110                     1115                     1120
            Arg Gly Ser Gly Lys Ser Asn Val Gly Ala Ser Gly Asp His Asp Asp
                        1125                     1130                     1135
            Ser Ala Met Lys Thr Leu Arg Asn Lys Met Gly Lys Trp Cys Cys His
                        1140                     1145                     1150
            Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Lys Val Gly Ala Trp
                        1155                     1160                     1165
            Gly Asp Tyr Asp Asp Ser Ala Phe Met Glu Pro Arg Tyr His Val Arg
                        1170                     1175                     1180
            Gly Glu Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val
            1185                     1190                     1195                     1200
            Pro Arg Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys
                        1205                     1210                     1215
            Lys Asp Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly
                        1220                     1225                     1230
            Asn Ser Glu Val Val Lys Leu Leu Leu Asp Arg Arg Cys Gln Leu Asn
                        1235                     1240                     1245
            Val Leu Asp Asn Lys Lys Arg Thr Ala Leu Ile Lys Ala Val Gln Cys
                        1250                     1255                     1260
            Gln Glu Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro
```

```
      1265                 1270                 1275                 1280
Asn Ile Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Ile Tyr
                  1285                 1290                 1295
Asn Glu Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp
            1300                 1305                 1310
Ile Glu Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Val
            1315                 1320                 1325
His Glu Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala
            1330                 1335                 1340
Asn Leu Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala
      1345                 1350                 1355                 1360
Val Cys Cys Gly Ser Ala Ser Ile Val Ser Leu Leu Leu Glu Gln Asn
                  1365                 1370                 1375
Ile Asp Val Ser Ser Gln Asp Leu Ser Gly Gln Thr Ala Arg Glu Tyr
            1380                 1385                 1390
Ala Val Ser Ser His His His Val Ile Cys Gln Leu Leu Ser Asp Tyr
            1395                 1400                 1405
Lys Glu Lys Gln Met Leu Lys Ile Ser Ser Glu Asn Ser Asn Pro Glu
      1410                 1415                 1420
Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Phe Lys Gly
1425                 1430                 1435                 1440
Ser Glu Asn Ser Gln Pro Glu Lys Met Ser Gln Glu Pro Glu Ile Asn
                  1445                 1450                 1455
Lys Asp Gly Asp Arg Glu Val Glu Glu Glu Met Lys Lys His Glu Ser
            1460                 1465                 1470
Asn Asn Val Gly Leu Leu Glu Asn Leu Thr Asn Gly Val Thr Ala Gly
            1475                 1480                 1485
Asn Gly Asp Asn Gly Leu Ile Pro Gln Arg Lys Ser Arg Thr Pro Glu
      1490                 1495                 1500
Asn Gln Gln Phe Pro Asp Asn Glu Ser Glu Glu Tyr His Arg Ile Cys
1505                 1510                 1515                 1520
Glu Leu Val Ser Asp Tyr Lys Glu Lys Gln Met Pro Lys Tyr Ser Ser
                  1525                 1530                 1535
Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu Glu Glu
            1540                 1545                 1550
Ser Gln Arg Leu Glu Gly Ser Glu Asn Gly Gln Pro Glu Lys Arg Ser
            1555                 1560                 1565
Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Leu Glu Asn Phe
      1570                 1575                 1580
Met Ala Ile Glu Glu Met Lys Lys His Gly Ser Thr His Val Gly Phe
1585                 1590                 1595                 1600
Pro Glu Asn Leu Thr Asn Gly Ala Thr Ala Gly Asn Gly Asp Asp Gly
                  1605                 1610                 1615
Leu Ile Pro Pro Arg Lys Ser Arg Thr Pro Glu Ser Gln Gln Phe Pro
            1620                 1625                 1630
Asp Thr Glu Asn Glu Glu Tyr His Ser Asp Glu Gln Asn Asp Thr Gln
            1635                 1640                 1645
Lys Gln Phe Cys Glu Glu Gln Asn Thr Gly Ile Leu His Asp Glu Ile
      1650                 1655                 1660
Leu Ile His Glu Glu Lys Gln Ile Glu Val Val Glu Lys Met Asn Ser
1665                 1670                 1675                 1680
Glu Leu Ser Leu Ser Cys Lys Lys Glu Lys Asp Ile Leu His Glu Asn
                  1685                 1690                 1695
Ser Thr Leu Arg Glu Glu Ile Ala Met Leu Arg Leu Glu Leu Asp Thr
            1700                 1705                 1710
Met Lys His Gln Ser Gln Leu
            1715
```

```
<210> 379
<211> 656
<212> PRT
<213> Homo sapien

<400> 379
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1               5                   10                  15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
            20                  25                  30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
            35                  40                  45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
    50                  55                  60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65                  70                  75                  80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
            85                  90                  95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
            100                 105                 110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
            115                 120                 125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
    130                 135                 140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145                 150                 155                 160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
            165                 170                 175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
            180                 185                 190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
            195                 200                 205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
    210                 215                 220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225                 230                 235                 240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
            245                 250                 255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
            260                 265                 270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
            275                 280                 285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
    290                 295                 300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305                 310                 315                 320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
            325                 330                 335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
            340                 345                 350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
            355                 360                 365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
    370                 375                 380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385                 390                 395                 400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
            405                 410                 415
```

```
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
        420             425             430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
        435             440             445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
450             455             460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465             470             475             480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
            485             490             495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
            500             505             510
Asn Gly Gln Pro Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys
        515             520             525
Lys His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly
        530             535             540
Ala Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser
545             550             555             560
Arg Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr
            565             570             575
His Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln
            580             585             590
Asn Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln
        595             600             605
Ile Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys
    610             615             620
Lys Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile
625             630             635             640
Ala Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
            645             650             655
```

```
        <210> 380
        <211> 671
        <212> PRT
        <213> Homo sapien

        <400> 380
Met Val Val Glu Val Asp Ser Met Pro Ala Ala Ser Ser Val Lys Lys
1               5               10              15
Pro Phe Gly Leu Arg Ser Lys Met Gly Lys Trp Cys Cys Arg Cys Phe
            20              25              30
Pro Cys Cys Arg Glu Ser Gly Lys Ser Asn Val Gly Thr Ser Gly Asp
        35              40              45
His Asp Asp Ser Ala Met Lys Thr Leu Arg Ser Lys Met Gly Lys Trp
        50              55              60
Cys Arg His Cys Phe Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val
65              70              75              80
Gly Ala Ser Gly Asp His Asp Asp Ser Ala Met Lys Thr Leu Arg Asn
            85              90              95
Lys Met Gly Lys Trp Cys Cys His Cys Phe Pro Cys Cys Arg Gly Ser
        100             105             110
Gly Lys Ser Lys Val Gly Ala Trp Gly Asp Tyr Asp Asp Ser Ala Phe
        115             120             125
Met Glu Pro Arg Tyr His Val Arg Gly Glu Asp Leu Asp Lys Leu His
    130             135             140
Arg Ala Ala Trp Trp Gly Lys Val Pro Arg Lys Asp Leu Ile Val Met
145             150             155             160
Leu Arg Asp Thr Asp Val Asn Lys Lys Asp Lys Gln Lys Arg Thr Ala
```

```
                    165                    170                    175
Leu His Leu Ala Ser Ala Asn Gly Asn Ser Glu Val Val Lys Leu Leu
            180                    185                    190
Leu Asp Arg Arg Cys Gln Leu Asn Val Leu Asp Asn Lys Lys Arg Thr
            195                    200                    205
Ala Leu Ile Lys Ala Val Gln Cys Gln Glu Asp Glu Cys Ala Leu Met
    210                    215                    220
Leu Leu Glu His Gly Thr Asp Pro Asn Ile Pro Asp Glu Tyr Gly Asn
225                    230                    235                    240
Thr Thr Leu His Tyr Ala Ile Tyr Asn Glu Asp Lys Leu Met Ala Lys
                245                    250                    255
Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu Ser Lys Asn Lys His Gly
                260                    265                    270
Leu Thr Pro Leu Leu Leu Gly Val His Glu Gln Lys Gln Gln Val Val
            275                    280                    285
Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu Asn Ala Leu Asp Arg Tyr
    290                    295                    300
Gly Arg Thr Ala Leu Ile Leu Ala Val Cys Cys Gly Ser Ala Ser Ile
305                    310                    315                    320
Val Ser Leu Leu Leu Glu Gln Asn Ile Asp Val Ser Ser Gln Asp Leu
                325                    330                    335
Ser Gly Gln Thr Ala Arg Glu Tyr Ala Val Ser Ser His His His Val
            340                    345                    350
Ile Cys Gln Leu Leu Ser Asp Tyr Lys Glu Lys Gln Met Leu Lys Ile
            355                    360                    365
Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp Leu Lys Leu Thr Ser Glu
    370                    375                    380
Glu Glu Ser Gln Arg Phe Lys Gly Ser Glu Asn Ser Gln Pro Glu Lys
385                    390                    395                    400
Met Ser Gln Glu Pro Glu Ile Asn Lys Asp Gly Asp Arg Glu Val Glu
            405                    410                    415
Glu Glu Met Lys Lys His Glu Ser Asn Asn Val Gly Leu Leu Glu Asn
            420                    425                    430
Leu Thr Asn Gly Val Thr Ala Gly Asn Gly Asp Asn Gly Leu Ile Pro
        435                    440                    445
Gln Arg Lys Ser Arg Thr Pro Glu Asn Gln Gln Phe Pro Asp Asn Glu
    450                    455                    460
Ser Glu Glu Tyr His Arg Ile Cys Glu Leu Val Ser Asp Tyr Lys Glu
465                    470                    475                    480
Lys Gln Met Pro Lys Tyr Ser Ser Glu Asn Ser Asn Pro Glu Gln Asp
            485                    490                    495
Leu Lys Leu Thr Ser Glu Glu Glu Ser Gln Arg Leu Glu Gly Ser Glu
            500                    505                    510
Asn Gly Gln Pro Glu Lys Arg Ser Gln Glu Pro Glu Ile Asn Lys Asp
        515                    520                    525
Gly Asp Arg Glu Leu Glu Asn Phe Met Ala Ile Glu Glu Met Lys Lys
    530                    535                    540
His Gly Ser Thr His Val Gly Phe Pro Glu Asn Leu Thr Asn Gly Ala
545                    550                    555                    560
Thr Ala Gly Asn Gly Asp Asp Gly Leu Ile Pro Pro Arg Lys Ser Arg
                565                    570                    575
Thr Pro Glu Ser Gln Gln Phe Pro Asp Thr Glu Asn Glu Glu Tyr His
            580                    585                    590
Ser Asp Glu Gln Asn Asp Thr Gln Lys Gln Phe Cys Glu Glu Gln Asn
        595                    600                    605
Thr Gly Ile Leu His Asp Glu Ile Leu Ile His Glu Glu Lys Gln Ile
    610                    615                    620
Glu Val Val Glu Lys Met Asn Ser Glu Leu Ser Leu Ser Cys Lys Lys
```

```
625                    630                   635                   640
Glu Lys Asp Ile Leu His Glu Asn Ser Thr Leu Arg Glu Glu Ile Ala
                    645                   650                   655
Met Leu Arg Leu Glu Leu Asp Thr Met Lys His Gln Ser Gln Leu
                660                   665                   670
```

```
        <210> 381
        <211> 251
        <212> DNA
        <213> Homo sapien

        <400> 381
        ggagaagcgt ctgctggggc aggaaggggt ttccctgccc tctcacctgt ccctcaccaa      60
        ggtaacatgc ttcccctaag ggtatcccaa cccagggggcc tcaccatgac ctctgagggg     120
        ccaatatccc aggagaagca ttggggagtt gggggggcaggt gaaggaccca ggactcacac    180
        atcctgggcc tccaaggcag aggagagggt cctcaagaag gtcaggagga aaatccgtaa      240
        caagcagtca g                                                          251
```

```
<210> 382
<211> 3279
<212> DNA
<213> Homo sapiens

<400> 382
cttcctgcag cccccatgct ggtgaggggc acgggcagga acagtggacc caacatggaa 60
atgctggagg gtgtcaggaa gtgatcgggc tctggggcag ggaggagggg tggggagtgt 120
cactgggagg ggacatcctg cagaaggtag gagtgagcaa acacccgctg caggggaggg 180
gagagccctg cggcacctgg gggagcagag ggagcagcac ctgcccaggc ctgggaggag 240
gggcctggag ggcgtgagga ggagcgaggg ggctgcatgg ctggagtgag ggatcagggg 300
cagggcgcga gatggcctca cacagggaag agagggcccc tcctgcaggg cctcacctgg 360
gccacaggag gacactgctt ttcctctgag gagtcaggag ctgtggatgg tgctggacag 420
aagaaggaca gggcctggct caggtgtcca gaggctgtcg ctggcttccc tttgggatca 480
gactgcaggg agggaggggcg gcagggttgt gggggggagtg acgatgagga tgacctgggg 540
gtggctccag gccttgcccc tgcctgggcc ctcacccagc ctccctcaca gtctcctggc 600
cctcagtctc tcccctccac tccatcctcc atctggcctc agtgggtcat tctgatcact 660
gaactgacca tacccagccc tgcccacggc cctccatggc tccccaatgc cctggagagg 720
ggacatctag tcagagagta gtcctgaaga ggtggcctct gcgatgtgcc tgtgggggca 780
gcatcctgca gatggtcccg gccctcatcc tgctgacctg tctgcaggga ctgtcctcct 840
ggaccttgcc ccttgtgcag gagctggacc ctgaagtccc ctccccatag gccaagactg 900
gagccttgtt ccctctgttg gactccctgc ccatattctt gtgggagtgg gttctggaga 960
catttctgtc tgttcctgag agctgggaat tgctctcagt catctgcctg cgcggttctg 1020
agagatggag ttgcctaggc agttattggg gccaatcttt ctcactgtgt ctctcctcct 1080
ttaccttag ggtgattctg ggggtccact tgtctgtaat ggtgtgcttc aaggtatcac 1140
atcatggggc cctgagccat gtgccctgcc tgaaaagcct gctgtgtaca ccaaggtggt 1200
gcattaccgg aagtggatca aggacaccat cgcagccaac ccctgagtgc ccctgtccca 1260
cccctacctc tagtaaattt aagtccacct cacgttctgg catcacttgg cctttctgga 1320
tgctggacac ctgaagcttg gaactcacct ggccgaagct cgagcctcct gagtcctact 1380
gacctgtgct ttctggtgtg gagtccaggg ctgctaggaa aaggaatggg cagacacagg 1440
tgtatgccaa tgtttctgaa atgggtataa tttcgtcctc tccttcggaa cactggctgt 1500
ctctgaagac ttctcgctca gtttcagtga ggacacacac aaagacgtgg gtgaccatgt 1560
tgtttgtggg gtgcagagat gggaggggtg gggcccaccc tggaagagtg acagtgaca 1620
caaggtggac actctctaca gatcactgag gataagctgg agccacaatg catgaggcac 1680
acacacagca aggttgacgc tgtaaacata gcccacgctg tcctgggggc actgggaagc 1740
ctagataagg ccgtgagcag aaagaagggg aggatcctcc tatgttgttg aaggagggac 1800
taggggagaa aactgaaagc tgattaatta caggaggttt gttcaggtcc cccaaaccac 1860
cgtcagattt gatgatttcc tagcaggact tacagaaata aagagctatc atgctgtggt 1920
ttattatggt ttgttacatt gataggatac atactgaaat cagcaaacaa aacagatgta 1980
tagattagag tgtggagaaa acagaggaaa acttgcagtt acgaagactg gcaacttggc 2040
```

```
tttactaagt tttcagactg gcaggaagtc aaacctatta ggctgaggac cttgtggagt 2100
gtagctgatc cagctgatag aggaactagc caggtggggg cctttccctt tggatggggg 2160
gcatatccga cagttattct ctccaagtgg agacttacgg acagcatata attctccctg 2220
caaggatgta tgataaatatg tacaaagtaa ttccaactga ggaagctcac ctgatcctta 2280
gtgtccaggg tttttactgg gggtctgtag gacgagtatg gagtacttga ataattgacc 2340
tgaagtcctc agacctgagg ttccctagag ttcaaacaga tacagcatgg tccagagtcc 2400
cagatgtaca aaaacaggga ttcatcacaa atcccatctt tagcatgaag ggtctggcat 2460
ggcccaaggc cccaagtata tcaaggcact tgggcagaac atgccaagga atcaaatgtc 2520
atctcccagg agttattcaa gggtgagccc tttacttggg atgtacaggc tttgagcagt 2580
gcagggctgc tgagtcaacc tttattgta caggggatga gggaaaggga gaggatgagg 2640
aagcccccct ggggatttgg tttggtcttg tgatcaggtg gtctatgggg ctatccctac 2700
aaagaagaat ccagaaatag gggcacattg aggaatgata ctgagcccaa agagcattca 2760
atcattgttt tatttgcctt cttttcacac cattggtgag ggagggatta ccaccctggg 2820
gttatgaaga tggttgaaca ccccacacat agcaccggag atatgagatc aacagtttct 2880
tagccataga gattcacagc ccagagcagg aggacgctgc acaccatgca ggatgacatg 2940
ggggatgcgc tcgggattgg tgtgaagaag caaggactgt tagaggcagg ctttatagta 3000
acaagacggt ggggcaaact ctgatttccg tgggggaatg tcatggtctt gctttactaa 3060
gttttgagac tggcaggtag tgaaactcat taggctgaga accttgtgga atgcagctga 3120
cccagctgat agaggaagta gccaggtggg agcctttccc agtgggtgtg ggacatatct 3180
ggcaagattt tgtggcactc ctggttacag atactgggggc agcaaataaa actgaatctt 3240
gttttcagac cttaaaaaaa aaaaaaaaaa aaaagtttt                         3279
```

<210> 383
<211> 154
<212> PRT
<213> Homo sapiens

<400> 383

```
Met Ala Gly Val Arg Asp Gln Gly Gln Gly Ala Arg Trp Pro His Thr
                    5                  10                  15

Gly Lys Arg Gly Pro Leu Leu Gln Gly Leu Thr Trp Ala Thr Gly Gly
               20                  25                  30

His Cys Phe Ser Ser Glu Glu Ser Gly Ala Val Asp Gly Ala Gly Gln
               35                  40                  45

Lys Lys Asp Arg Ala Trp Leu Arg Cys Pro Glu Ala Val Ala Gly Phe
       50                  55                  60

Pro Leu Gly Ser Asp Cys Arg Glu Gly Gly Arg Gln Gly Cys Gly Gly
65                  70                  75                  80

Ser Asp Asp Glu Asp Asp Leu Gly Val Ala Pro Gly Leu Ala Pro Ala
                   85                  90                  95

Trp Ala Leu Thr Gln Pro Pro Ser Gln Ser Pro Gly Pro Gln Ser Leu
               100                 105                 110

Pro Ser Thr Pro Ser Ser Ile Trp Pro Gln Trp Val Ile Leu Ile Thr
           115                 120                 125

Glu Leu Thr Ile Pro Ser Pro Ala His Gly Pro Pro Trp Leu Pro Asn
       130                 135                 140

Ala Leu Glu Arg Gly His Leu Val Arg Glu
145                 150
```

```
<210> 384
<211> 557
<212> DNA
<213> Homo sapiens

<400> 384
ggatcctcta gagcggccgc ctactactac taaattcgcg gccgcgtcga cgaagaagag 60
aaagatgtgt tttgttttgg actctctgtg gtcccttcca atgctgtggg tttccaacca 120
ggggaagggt cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggt 180
tctgcctcct ggccaagcag gctggtttgc aagaatgaaa tgaatgattc tacagctagg 240
acttaacctt gaaatggaaa gtcttgcaat cccatttgca ggatccgtct gtgcacatgc 300
ctctgtagag agcagcattc ccagggacct tggaaacagt tggcactgta aggtgcttgc 360
-tccccaagac acatcctaaa aggtgttgta atggtgaaaa cgtcttcctt ctttattgcc 420
ccttcttatt tatgtgaaca actgtttgtc ttttttttgta tctttttttaa actgtaaagt 480
tcaattgtga aaatgaatat catgcaaata aattatgcga tttttttttc aaagtaaaaa 540
aaaaaaaaaa aaaaaaa                                                   557


<210> 385
<211> 337
<212> DNA
<213> Homo sapiens

<400> 385
ttcccaggtg atgtgcgagg gaagacacat ttactatcct tgatggggct gattcctttta 60
gtttctctag cagcagatgg gttaggagga agtgacccaa gtggttgact cctatgtgca 120
tctcaaagcc atctgctgtc ttcgagtacg gacacatcat cactcctgca ttgttgatca 180
aaacgtggag gtgctttttcc tcagctaaga agcccttagc aaaagctcga atagacttag 240
tatcagacag gtccagtttc cgcaccaaca cctgctggtt ccctgtcgtg gtctggatct 300
ctttggccac caattccccc ttttccacat cccggca                            337


<210> 386
<211> 300
<212> DNA
<213> Homo sapiens

<400> 386
gggcccgcta ccggcccagg ccccgcctcg cgagtcctcc tccccgggtg cctgcccgca 60
gcccgctcgg cccagagggt gggcgcgggg ctgcctctac cggctggcgg ctgtaactca 120
gcgaccttgg cccgaaggct ctagcaagga cccaccgacc ccagccgcgg cggcggcggc 180
gcggactttg cccggtgtgt ggggcggagc ggactgcgtg tccgcggacg ggcagcgaag 240
atgttagcct tcgctgccag gaccgtggac cgatcccagg gctgtggtgt aacctcagcc 300


<210> 387
<211> 537
<212> DNA
<213> Homo sapiens

<400> 387
gggccgagtc gggcaccaag ggactctttg caggcttcct tcctcggatc atcaaggctg 60
ccccctcctg tgccatcatg atcagcacct atgagttcgg caaaagcttc ttccagaggc 120
tgaaccagga ccggcttctg gcggctgaa aggggcaagg aggcaaggac cccgtctctc 180
ccacggatgg ggagagggca ggaggagacc cagccaagtg ccttttcctc agcactgagg 240
gagggggctt gtttcccttc cctccggcg acaagctcca gggcagggct gtccctctgg 300
gcggcccagc acttcctcag acacaacttc ttcctgctgc tccagtcgtg gggatcatca 360
cttacccacc ccccaagttc aagaccaaat cttccagctg ccccccttcgt gtttccctgt 420
gtttgctgta gctgggcatg tctccaggaa ccaagaagcc ctcagcctgg tgtagtctcc 480
ctgacccttg ttaattcctt aagtctaaag atgatgaact tcaaaaaaaa aaaaaaa      537
```

```
<210> 388
<211> 520
<212> DNA
<213> Homo sapiens

<400> 388
aggataattt ttaaaccaat caaatgaaaa aaacaaacaa acaaaaaagg aaatgtcatg 60
tgaggttaaa ccagtttgca ttcccctaat gtggaaaaag taagaggact actcagcact 120
gtttgaagat tgcctcttct acagcttctg agaattgtgt tatttcactt gccaagtgaa 180
ggaccccctc cccaacatgc cccagcccac ccctaagcat ggtcccttgt caccaggcaa 240
ccaggaaact gctacttgtg gacctcacca gagaccagga gggtttggtt agctcacagg 300
acttcccca ccccagaaga ttagcatccc atactagact catactcaac tcaactaggc 360
tcatactcaa ttgatggtta ttagacaatt ccatttcttt ctggttatta taaacagaaa 420
atctttcctc ttctcattac cagtaaaggc tcttggtatc tttctgttgg aatgatttct 480
atgaacttgt cttattttaa tggtgggttt tttttctggt 520
```

```
<210> 389
<211> 365
<212> DNA
<213> Homo sapiens

<400> 389
cgttgcccca gtttgacaga aggaaaggcg gagcttattc aaagtctaga gggagtggag 60
gagttaaggc tggatttcag atctgcctgg ttccagccgc agtgtgccct ctgctccccc 120
aacgactttc caaataatct caccagcgcc ttccagctca ggcgtcctag aagcgtcttg 180
aagcctatgg ccagctgtct ttgtgttccc tctcacccgc ctgtcctcac agctgagact 240
cccaggaaac cttcagacta ccttcctctg ccttcagcaa ggggcgttgc ccacattctc 300
tgagggtcag tggaagaacc tagactccca ttgctagagg tagaaagggg aagggtgctg 360
gggag 365
```

```
<210> 390
<211> 221
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(221)
<223> n = A,T,C or G

<400> 390
tgcctctcca tcctggcccc gacttctctg tcaggaaagt ggggatggac cccatctgca 60
tacacggntt ctcatgggtg tggaacatct ctgcttgcgg tttcaggaag gcctctggct 120
gctctangag tctgancnga ntcgttgccc cantntgaca naaggaaagg cggagcttat 180
tcaaagtcta gagggagtgg aggagttaag gctggatttc a 221
```

```
<210> 391
<211> 325
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(325)
<223> n = A,T,C or G

<400> 391
```

```
tggagcaggt cccgaggcct ccctagagcc tggggccgac tctgtgncga tgcangcttt  60
ctctcgcgcc cagcctggag ctgctcctgg catctaccaa caatcagncg aggcgagcag 120
tagccagggc actgctgcca acagccagtc cnnataccat catgtnaccc ggtgngctct 180
naanttngat ntccanagcc ctacccatcn tagttctgct ctcccaccgg ntaccagccc 240
cactgcccag gaatcctaca gccagtaccc tgtcccgacg tctctaccta ccagtacgat 300
gagacctccg gctactacta tgacc                                       325
```

`<210> 392`
`<211> 277`
`<212> DNA`
`<213> Homo sapiens`

`<220>`
`<221> misc_feature`
`<222> (1)...(277)`
`<223> n = A,T,C or G`

`<400> 392`
```
atattgttta actccttcct ttatatcttt taacattttc atggngaaag gttcacatct  60
agtctcactt nggcnagngn ctcctacttg agtctcttcc ccggcctgnn ccagtngnaa 120
antaccanga accgncatgn cttaanaacn ncctggtttn tgggttnntc aatgactgca 180
tgcagtgcac caccctgtcc actacgtgat gctgtaggat taaagtctca cagtgggcgg 240
ctgaggatac agcgccgcgt cctgtgttgc tggggaa                          277
```

`<210> 393`
`<211> 566`
`<212> DNA`
`<213> Homo sapiens`

`<400> 393`
```
actagtccag tgtggtggaa ttcgcggccg cgtcgacgga caggtcagct gtctggctca  60
gtgatctaca ttctgaagtt gtctgaaaat gtcttcatga ttaaattcag cctaaacgtt 120
ttgccgggaa cactgcagag acaatgctgt gagtttccaa ccttagccca tctgcgggca 180
gagaaggtct agtttgtcca tcagcattat catgatatca ggactggtta cttggttaag 240
gaggggtcta ggagatctgt cccttttaga gacaccttac ttataatgaa gtatttggga 300
gggtggtttt caaaagtaga aatgtcctgt attccgatga tcatcctgta aacattttat 360
catttattaa tcatccctgc ctgtgtctat tattatattc atatctctac gctggaaact 420
ttctgcctca atgtttactg tgcctttgtt tttgctagtt tgtgttgttg aaaaaaaaaa 480
cattctctgc ctgagtttta atttttgtcc aaagttattt taatctatac aattaaaagc 540
ttttgcctat caaaaaaaaa aaaaaa                                      566
```

`<210> 394`
`<211> 384`
`<212> DNA`
`<213> Homo sapiens`

`<220>`
`<221> misc_feature`
`<222> (1)...(384)`
`<223> n = A,T,C or G`

`<400> 394`
```
gaacatacat gtcccggcac ctgagctgca gtctgacatc atcgccatca cgggcctcgc  60
tgcaaattng gaccgggcca aggctggact gctggagcgt gtgaaggagc tacaggccna 120
gcaggaggac cgggctttaa ggagttttaa gctgagtgtc actgtagacc ccaaatacca 180
tcccaagatt atcgggagaa aggggggcagt aattacccaa atccggttgg agcatgacgt 240
gaacatccag tttcctgata aggacgatgg gaaccagccc caggaccaaa ttaccatcac 300
agggtacgaa aagaacacag aagctgccag ggatgctata ctgagaattg tgggtgaact 360
```

tgagcagatg gtttctgagg acgt   384

<210> 395
<211> 399
<212> DNA
<213> Homo sapiens

<400> 395
ggcaaaactg tgtgacctca ataagacctc gcagatccaa ggtcaagtat cagaagtgac 60
tctgaccttg gactccaaga cctacatcaa cagcctggct atattagatg atgagccagt 120
tatcagaggt ttcatcattg cggaaattgt ggagtctaag gaaatcatgg cctctgaagt 180
attcacgtct ttccagtacc ctgagttctc tatagagttg cctaacacag gcagaattgg 240
ccagctactt gtctgcaatt gtatcttcaa.gaataccctg gccatccctt tgactgacgt 300
caagttctct ttggaaagcc tgggcatctc ctcactacag acctctgacc atgggacggt 360
gcagcctggt gagaccatcc aatcccaaat aaaatgcac   399

<210> 396
<211> 403
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(403)
<223> n = A,T,C or G

<400> 396
tggagttntc agtgcaaaca agccataaag cttcagtagc aaattactgt ctcacagaaa 60
gacattttca acttctgctc cagctgctga taaaacaaat catgtgttta gcttgactcc 120
agacaaggac aacctgttcc ttcat`aactc tctagagaaa aaaggagtt gttagtagat 180
actaaaaaaa gtggatgaat aatctggata tttttcctaa aaagattcct tgaaacacat 240
taggaaaatg gagggcctta tgatcagaat gctagaatta gtccattgtg ctgaagcagg 300
gtttaggga gggagtgagg gataaaagaa ggaaaaaaag aagagtgaga aaacctattt 360
atcaaagcag gtgctatcac tcaatgttag gccctgctct ttt   403

<210> 397
<211> 100
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(100)
<223> n = A,T,C or G

<400> 397
actagtncag tgtggtggaa ttcgcggccg cgtcgaccta naanccatct ctatagcaaa 60
tccatccccg ctcctggttg gtnacagaat gactgacaaa   100

<210> 398
<211> 278
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(278)
<223> n = A,T,C or G

138

```
<400> 398
gcggccgcgt cgacagcagt tccgccagcg ctcgcccctg ggtggggatg tgctgcacgc 60
ccacctggac atctggaagt cagcggcctg gatgaaagag cggacttcac ctggggcgat 120
tcactactgt gcctcgacca gtgaggagag ctggaccgac agcgaggtgg actcatcatg 180
ctccgggcag cccatccacc tgtggcagtt cctcaaggag ttgctactca agccccacag 240
ctatggccgc ttcattangt ggctcaacaa ggagaagg                         278


<210> 399
<211> 298
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(298)
<223> n = A,T,C or G

<400> 399
acggaggtgg aggaagcgnc cctgggatcg anaggatggg tcctgncatt gaccncctcn 60
ggggtgccng catggagcgc atgggcgcgg gcctgggcca cggcatggat cgcgtgggct 120
ccgagatcga gcgcatgggc ctggtcatgg accgcatggg ctccgtggag cgcatgggct 180
ccggcattga gcgcatgggc ccgctgggcc tcgaccacat ggcctccanc attgancgca 240
tgggccagac catggagcgc attggctctg gcgtggagcn catgggtgcc ggcatggg    298


<210> 400
<211> 548
<212> DNA
<213> Homo sapiens

<400> 400
acatcaacta cttcctcatt ttaaggtatg gcagttccct tcatcccctt ttcctgcctt 60
gtacatgtac atgtatgaaa tttccttctc ttaccgaact ctctccacac atcacaaggt 120
caaagaacca cacgcttaga agggtaagag ggcaccctat gaaatgaaat ggtgatttct 180
tgagtctctt ttttccacgt ttaaggggcc atggcaggac ttagagttgc gagttaagac 240
tgcagagggc tagagaatta tttcatacag gctttgaggc cacccatgtc acttatcccg 300
tataccctct caccatcccc ttgtctactc tgatgccccc aagatgcaac tgggcagcta 360
gttggcccca taattctggg cctttgttgt ttgttttaat tacttgggca tcccaggaag 420
ctttccagtg atctcctacc atgggccccc ctcctgggat caagcccctc ccaggccctg 480
tccccagccc ctcctgcccc agcccacccg cttgccttgg tgctcagccc tcccattggg 540
agcaggtt                                                          548


<210> 401
<211> 355
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(355)
<223> n = A,T,C or G

<400> 401
actgtttcca tgttatgttt ctacacattg ctacctcagt gctcctggaa acttagcttt 60
tgatgtctcc aagtagtcca ccttcattta actctttgaa actgtatcat ctttgccaag 120
taagagtggt ggcctatttc agctgctttg acaaaatgac tggctcctga cttaacgttc 180
tataaatgaa tgtgctgaag caaagtgccc atggtggcgg cgaagaagan aaagatgtgt 240
tttgttttgg actctctgtg gtcccttcca atgctgnggg tttccaacca ggggaagggt 300
```

139

```
cccttttgca ttgccaagtg ccataaccat gagcactact ctaccatggn tctgc      355
```

```
<210> 402
<211> 407
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(407)
<223> n = A,T,C or G

<400> 402
atggggcaag ctggataaag aaccaagacc cactggagta tgctgtcttc aagaaaccca 60
tctcacatgc ggtggcatac ataggctcaa aataaaggaa tggagaaaaa tatttcaagc 120
aaatggaaaa cagaaaaaag caggtgttgc actcctactt tctgacaaaa cagactatgc 180
gaataaagat aaaaaagaga aggacattac aaaggtggtc ctgacctttg ataaatctca 240
ttgcttgata ccaacctggg ctgttttaat tgcccaaacc aaaaggataa tttgctgagg 300
ttgtggagct tctcccctgc agagagtccc tgatctccca aaatttggtt gagatgtaag 360
gntgattttg ctgacaactc cttttctgaa gttttactca tttccaa              407
```

```
<210> 403
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 403
cagtatttat agccnaactg aaaagctagt agcaggcaag tctcaaatcc aggcaccaaa 60
tcctaagcaa gagccatggc atggtgaaaa tgcaaaagga gagtctggcc aatctacaaa 120
tagagaacaa gacctactca gtcatgaaca aaaaggcaga caccaacatg gatctcatgg 180
gggattggat attgtaatta tagagcagga agatgacagt gatcgtcatt tggcacaaca 240
tcttaacaac gaccgaaacc cattatttac ataaacctcc attcggtaac catgttgaaa 300
gga                                                                303
```

```
<210> 404
<211> 225
<212> DNA
<213> Homo sapiens

<400> 404
aagtgtaact tttaaaaatt tagtggattt tgaaaattct tagaggaaag taaaggaaaa 60
attgttaatg cactcattta cctttacatg gtgaaagttc tctcttgatc ctacaaacag 120
acattttcca ctcgtgtttc catagttgtt aagtgtatca gatgtgttgg gcatgtgaat 180
ctccaagtgc ctgtgtaata aataaagtat ctttatttca ttcat                225
```

```
<210> 405
<211> 334
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(334)
```

```
<223> n = A,T,C or G

<400> 405
gagctgttat actgtgagtt ctactaggaa atcatcaaat ctgagggttg tctggaggac 60
ttcaatacac ctccccccat agtgaatcag cttccagggg gtccagtccc tctccttact 120
tcatccccat cccatgccaa aggaagaccc tccctccttg gctcacagcc ttctctaggc 180
ttcccagtgc ctccaggaca gagtgggtta tgttttcagc tccatccttg ctgtgagtgt 240
ctggtgcggt tgtgcctcca gcttctgctc agtgcttcat ggacagtgtc cagcccatgt 300
cactctccac tctctcanng tggatcccac ccct                               334


<210> 406
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 406
tttcatacct aatgagggag ttganatnac atnnaaccag gaaatgcatg gatctcaang 60
gaaacaaaca cccaataaac tcggagtggc agactgacaa ctgtgagaca tgcacttgct 120
acnaaacaca aatttnatgt tgcacccttg tttctacacc tgtgggttat gacaaagaca 180
actgccaaag aatnttcaag aaggaggact gccant                             216


<210> 407
<211> 413
<212> DNA
<213> Homo sapiens

<400> 407
gctgacttgc tagtatcatc tgcattcatt gaagcacaag aacttcatgc cttgactcat 60
gtaaatgcaa taggattaaa aaataaattt gatatcacat ggaaacagac aaaaaatatt 120
gtacaacatt gcacccagtg tcagattcta cacctggcca ctcaggaagc aagagttaat 180
cccagaggtc tatgtcctaa tgtgttatgg caaatggatg tcatgcacgt accttcattt 240
ggaaaattgt catttgtcca tgtgacagtt gatacttatt cacatttcat atgggcaacc 300
tgccagacag gagaaagtct tcccatgtta aaagacattt attatcttgt tttcctgtca 360
tgggagttcc agaaaaagtt aaaacagaca atgggccagg ttctgtagta aag          413


<210> 408
<211> 183
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(183)
<223> n = A,T,C or G

<400> 408
ggagctngcc ctcaattcct ccatntctat gttancatat ttaatgtctt ttgnnattaa 60
tncttaacta gttaatcctt aaagggctan ntaatcctta actagtccct ccattgtgag 120
cattatcctt ccagtattcn ccttctnttt tatttactcc ttcctggcta cccatgtact 180
ntt                                                                 183


<210> 409
<211> 250
```

141

```
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(250)
<223> n = A,T,C or G

<400> 409
cccacgcatg ataagctctt tatttctgta agtcctgcta ggaaatcatc aaatctgacg 60
gtggtttggg ggacctgaac aaacctcctg taattaatca gctttcagtt tctcccccta 120
gtccctcctt caacaacata ggaggatcct ccccttcttt ctgctcacgg ccttatctag 180
gcttcccagt gcccccagga cagcgtgggc tatgtttaca gcgcntcctt gctggggggg 240
ggccntatgc                                                        250


<210> 410
<211> 306
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(306)
<223> n = A,T,C or G

<400> 410
ggctggtttg caagaatgaa atgaatgatt ctacagctag gacttaacct tgaaatggaa 60
agtcttgcaa tcccatttgc aggatccgtc tgtgcacatg cctctgtaga gagcagcatt 120
cccagggacc ttggaaacag ttggcactgt aaggtgcttg ctccccaaga cacatcctaa 180
aaggtgttgt aatggtgaaa accgcttcct tctttattgc cccttcttat ttatgtgaac 240
nactggttgg ctttttttgn atcttttta aactggaaag ttcaattgng aaaatgaata 300
tcntgc                                                            306


<210> 411
<211> 261
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(261)
<223> n = A,T,C or G

<400> 411
agagatattn cttaggtnaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatcttttg tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggngaggcaa a                                            261


<210> 412
<211> 241
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(241)
```

<223> n = A,T,C or G

<400> 412
gttcaatgtt acctgacatt tctacaacac cccactcacc gatgtattcg ttgcccagtg 60
ggaacatacc agcctgaatt tggaaaaaat aattgtgttt cttgcccagg aaatactacg 120
actgactttg atggctccac aaacataacc cagtgtaaaa acagaagatg tggaggggag 180
ctgggagatt tcactgggta cattgaattc ccaaactacc cangcaatta cccagccaac 240
a   241

<210> 413
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 413
aactcttaca atccaagtga ctcatctgtg tgcttgaatc ctttccactg tctcatctcc 60
ctcatccaag tttctagtac cttctctttg ttgtgaagga taatcaaact gaacaacaaa 120
aagtttactc tcctcatttg gaacctaaaa actctcttct tcctgggtct gagggctcca 180
agaatccttg aatcanttct cagatcattg gggacaccan atcaggaacc t   231

<210> 414
<211> 234
<212> DNA
<213> Homo sapiens

<400> 414
actgtccatg aagcactgag cagaagctgg aggcacaacg caccagacac tcacagcaag 60
gatggagctg aaaacataac ccactctgtc ctggaggcac tgggaagcct agagaaggct 120
gtgagccaag gagggagggt cttcctttgg catgggatgg ggatgaagta aggagaggga 180
ctggaccccc tggaagctga ttcactatgg ggggaggtgt attgaagtcc tcca   234

<210> 415
<211> 217
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(217)
<223> n = A,T,C or G

<400> 415
gcataggatt aagactgagt atcttttcta cattctttta actttctaag gggcacttct 60
caaaacacag accaggtagc aaatctccac tgctctaagg ntctcaccac cactttctca 120
cacctagcaa tagtagaatt cagtcctact tctgaggcca gaagaatggt tcagaaaaat 180
antggattat aaaaaataac aattaagaaa aataatc   217

<210> 416
<211> 213
<212> DNA
<213> Homo sapiens

<220>

143

<221> misc_feature
<222> (1)...(213)
<223> n = A,T,C or G

<400> 416
atgcatatnt aaagganact gcctcgcttt tagaagacat ctggnctgct ctctgcatga 60
ggcacagcag taaagctctt tgattcccag aatcaagaac tctccccttc agactattac 120
cgaatgcaag gtggttaatt gaaggccact aattgatgct caaatagaag gatattgact 180
atattggaac agatggagtc tctactacaa aag   213

<210> 417
<211> 303
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(303)
<223> n = A,T,C or G

<400> 417
nagtcttcag gcccatcagg gaagttcaca ctggagagaa gtcatacata tgtactgtat 60
gtgggaaagg ctttactctg agttcaaatc ttcaagccca tcagagagtc cacactggag 120
agaagccata caaatgcaat gagtgtggga agagcttcag gagggattcc cattatcaag 180
ttcatctagt ggtccacaca ggagagaaac cctataaatg tgagatatgt gggaagggct 240
tcantcaaag ttcgtatctt caaatccatc ngaaggncca cagtatanan aaacctttta 300
agt   303

<210> 418
<211> 328
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(328)
<223> n = A,T,C or G

<400> 418
tttttggcgg tggtggggca gggacgggac angagtctca ctctgttgcc caggctggag 60
tgcacaggca tgatctcggc tcactacaac ccctgcctcc catgtccaag cgattcttgt 120
gcctcagcct tccctgtagc tagaattaca ggcacatgcc accacaccca gctagttttt 180
gtattttttag tagagacagg gtttcaccat gttggccagg ctggtctcaa actcctnacc 240
tcagnggtca ggctggtctc aaactcctga cctcaagtga tctgcccacc tcagcctccc 300
aaagtgctan gattacaggc cgtgagcc   328

<210> 419
<211> 389
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(389)
<223> n = A,T,C or G

<400> 419
cctcctcaag acggcctgtg gtccgcctcc cggcaaccaa gaagcctgca gtgccatatg 60

144

```
acccctgagc catggactgg agcctgaaag gcagcgtaca ccctgctcct gatcttgctg 120
cttgtttcct ctctgtggct ccattcatag cacagttgtt gcactgaggc ttgtgcaggc 180
cgagcaaggc caagctggct caaagagcaa ccagtcaact ctgccacggt gtgccaggca 240
ccggttctcc agccaccaac ctcactcgct cccgcaaatg gcacatcagt tcttctaccc 300
taaaggtagg accaaagggc atctgctttt ctgaagtcct ctgctctatc agccatcacg 360
tggcagccac tcnggctgtg tcgacgcgg                                   389
```

```
<210> 420
<211> 408
<212> DNA
<213> Homo sapiens
```

```
<400> 420
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga caccttttccc actgaccccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg aagtgctatg acaaacctgg caagcccg              408
```

```
<210> 421
<211> 352
<212> DNA
<213> Homo sapiens
```

```
<220>
<221> misc_feature
<222> (1)...(352)
<223> n = A,T,C or G
```

```
<400> 421
gctcaaaaat cttttactg atnggcatgg ctacacaatc attgactatt acggaggcca 60
gaggagaatg aggcctggcc tgggagccct gtgcctacta naagcacatt agattatcca 120
ttcactgaca gaacaggtct ttttgggtc cttcttctcc accacnatat acttgcagtc 180
ctccttcttg aagattcttt ggcagttgtc tttgtcataa cccacaggtg tagaaacaag 240
ggtgcaacat gaaatttctg tttcgtagca agtgcatgtc tcacaagttg gcangtctgc 300
cactccgagt ttattgggtg tttgtttcct ttgagatcca tgcatttcct gg         352
```

```
<210> 422
<211> 337
<212> DNA
<213> Homo sapiens
```

```
<400> 422
atgccaccat gctggcaatg cagcgggcgg tcgaaggcct gcatatccag cccaagctgg 60
cgatgatcga cggcaaccgt tgcccgaagt tgccgatgcc agccgaagcg gtggtcaagg 120
gcgatagcaa ggtgccggcg atcgcggcgg cgtcaatcct ggccaaggtc agccgtgatc 180
gtgaaatggc agctgtcgaa ttgatctacc cgggttatgg catcggcggg cataagggct 240
atccgacacc ggtgcacctg gaagccttgc agcggctggg gccgacgccg attcaccgac 300
gcttcttccg ccggtacggc tggcctatga aaattat                         337
```

```
<210> 423
<211> 310
<212> DNA
<213> Homo sapiens
```

```
<220>
```

```
<221> misc_feature
<222> (1)...(310)
<223> n = A,T,C or G

<400> 423
gctcaaaaat cttttttactg atatggcatg gctacacaat cattgactat tagaggccag 60
aggagaatga ggcctggcct gggagccctg tgcctactan aagcncatta gattatccat 120
tcactgacag aacaggtctt ttttgggtcc ttcttctcca ccacgatata cttgcagtcc 180
tccttcttga agattctttg gcagttgtct ttgtcataac ccacaggtgt anaaacaagg 240
gtgcaacatg aaatttctgt ttcgtagcaa gtgcatgtct cacagttgtc aagtctgccc 300
tccgagttta                                                        310
```

```
<210> 424
<211> 370
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(370)
<223> n = A,T,C or G

<400> 424
gctcaaaaat cttttttactg ataggcatgg ctacacaatc attgactatt agaggccaga 60
ggagaatgag gcctggcctg ggagccctgt gcctactaga agcacattag attatccatt 120
cactgacaga acaggtcttt tttgggtcct tcttctccac cacgatatac ttgcagtcct 180
ccttcttgaa gattctttgg cagttgtctt tgtcataacc cacaggtgta gaaacatcct 240
ggttgaatct cctggaactc cctcattagg tatgaaatag catgatgcat tgcataaagt 300
cacgaaggtg gcaaagatca caacgctgcc cagganaaca ttcattgtga taagcaggac 360
tccgtcgacg                                                        370
```

```
<210> 425
<211> 216
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(216)
<223> n = A,T,C or G

<400> 425
aattgctatn ntttattttg ccactcaaaa taattaccaa aaaaaaaaaa tnttaaatga 60
taacaacnca acatcaaggn aaananaaca ggaatggntg actntgcata aatnggccga 120
anattatcca ttatnttaag ggttgacttc aggntacagc acacagacaa acatgcccag 180
gaggntntca ggaccgctcg atgtnttntg aggagg                          216
```

```
<210> 426
<211> 596
<212> DNA
<213> Homo sapiens

<400> 426
cttccagtga ggataaccct gttgccccgg gccgaggttc tccattaggc tctgattgat 60
tggcagtcag tgatggaagg gtgttctgat cattccgact gccccaaggg tcgctggcca 120
gctctctgtt ttgctgagtt ggcagtagga cctaatttgt taattaagag tagatggtga 180
gctgtccttg tattttgatt aacctaatgg ccttcccagc acgactcgga ttcagctgga 240
gacatcacgg caacttttaa tgaaatgatt tgaagggcca ttaagaggca cttcccgtta 300
```

```
ttaggcagtt catctgcact gataacttct tggcagctga gctggtcgga gctgtggccc 360
aaacgcacac ttggcttttg gttttgagat acaactctta atctttttagt catgcttgag 420
ggtggatggc cttttcagct ttaacccaat ttgcactgcc ttggaagtgt agccaggaga 480
atacactcat atactcgtgg gcttagaggc cacagcagat gtcattggtc tactgcctga 540
gtcccgctgg tcccatccca ggaccttcca tcggcgagta cctgggagcc cgtgct    596
```

<210> 427
<211> 107
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(107)
<223> n = A,T,C or G

<400> 427
```
gaagaattca agttaggttt attcaaaggg cttacngaga atcctanacc caggncccag 60
cccgggagca gccttanaga gctcctgttt gactgcccgg ctcagng             107
```

<210> 428
<211> 38
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(38)
<223> n = A,T,C or G

<400> 428
```
gaacttccna anaangactt tattcactat tttacatt                       38
```

<210> 429
<211> 544
<212> DNA
<213> Homo sapiens

<400> 429
```
ctttgctgga cggaataaaa gtggacgcaa gcatgacctc ctgatgaggg cgctgcattt 60
attgaagagc ggctgcagcc ctgcggttca gattaaaatc cgagaattgt atagacgccg 120
atatccacga actcttgaag gactttctga tttatccaca atcaaatcat cggttttcag 180
tttggatggt ggctcatcac ctgtagaacc tgacttggcc gtggctggaa tccactcgtt 240
gccttccact tcagttacac ctcactcacc atcctctcct gttggttctg tgctgcttca 300
agatactaag cccacatttg agatgcagca gccatctccc ccaattcctc ctgtccatcc 360
tgatgtgcag ttaaaaaatc tgcccttta tgatgtcctt gatgttctca tcaagcccac 420
gagtttagtt caaagcagta ttcagcgatt tcaagagaag ttttttattt ttgctttgac 480
acctcaacaa gttagagaga tatgcatatc cagggatttt ttgccaggtg gtaggagaga 540
ttat                                                            544
```

<210> 430
<211> 507
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(507)

```
<223> n = A,T,C or G

<400> 430
cttatcncaa tggggctccc aaacttggct gtgcagtgga aactccgggg gaattttgaa 60
gaacactgac acccatcttc caccccgaca ctctgattta attgggctgc agtgagaaca 120
gagcatcaat ttaaaaagct gcccagaatg ttntcctggg cagcgttgtg atctttgccn 180
ccttcgtgac tttatgcaat gcatcatgct atttcatacc taatgaggga gttccaggag 240
attcaaccag gatgtttcta cncctgtggg ttatgacaaa gacaactgcc aaagaatntt 300
caagaaggag gactgcaagt atatcgtggt ggagaagaag gacccaaaaa agacctgttc 360
tgtcagtgaa tggataatct aatgtgcttc tagtaggcac agggctccca ggccaggcct 420
cattctcctc tggcctctaa tagtcaatga ttgtgtagcc atgcctatca gtaaaaagat 480
ttttgagcaa aaaaaaaaaa aaaaaaa                                     507


<210> 431
<211> 392
<212> DNA
<213> Homo sapiens


<220>
<221> misc_feature
<222> (1)...(392)
<223> n = A,T,C or G


<400> 431
gaaaattcag aatggataaa aacaaatgaa gtacaaaata tttcagattt acatagcgat 60
aaacaagaaa gcacttatca ggaggactta caaatggaag tacactctan aaccatcatc 120
tatcatggct aaatgtgaga ttagcacagc tgtattattt gtacattgca aacacctaga 180
aagagatggg aaacaaaatc ccaggagttt tgtgtgtgga gtcctgggtt ttccaacaga 240
catcattcca gcattctgag attagggnga ttggggatca ttctggagtt ggaatgttca 300
acaaaagtga tgttgttagg taaaatgtac aacttctgga tctatgcaga cattgaaggt 360
gcaatgagtc tggctttac tctgctgttt ct                               392


<210> 432
<211> 387
<212> DNA
<213> Homo sapiens


<220>
<221> misc_feature
<222> (1)...(387)
<223> n = A,T,C or G


<400> 432
ggtatccnta cataatcaaa tatagctgta gtacatgttt tcattggngt agattaccac 60
aaatgcaagg caacatgtgt agatctcttg tcttattctt ttgtctataa tactgtattg 120
ngtagtccaa gctctcggna gtccagccac tgngaaacat gctcccttta gattaacctc 180
gtggacnctn ttgttgnatt gtctgaactg tagngccctg tattttgctt ctgtctgnga 240
attctgttgc ttctggggca tttccttgng atgcagagga ccaccacaca gatgacagca 300
atctgaattg ntccaatcac agctgcgatt aagacatact gaaatcgtac aggaccggga 360
acaacgtata gaacactgga gtccttt                                     387


<210> 433
<211> 281
<212> DNA
<213> Homo sapiens


<220>
<221> misc_feature
```

148

<210> (1)...(281)
<223> n = A,T,C or G

<400> 433
ttcaactagc anagaanact gcttcagggn gtgtaaaatg aaaggcttcc acgcagttat 60
ctgattaaag aacactaaga gagggacaag gctagaagcc gcaggatgtc tacactatag 120
caggcnctat ttgggttggc tggaggagct gtggaaaaca tggagagatt ggcgctggag 180
atcgccgtgg ctattcctcn ttgntattac accagngagg ntctctgtnt gcccactggt 240
tnnaaaaccg ntatacaata atgatagaat aggacacaca t 281

<210> 434
<211> 484
<212> DNA
<213> Homo sapiens

<400> 434
ttttaaaata agcatttagt gctcagtccc tactgagtac tctttctctc ccctcctctg 60
aatttaattc tttcaacttg caatttgcaa ggattacaca tttcactgtg atgtatattg 120
tgttgcaaaa aaaaaaaagt gtctttgttt aaaattactt ggtttgtgaa tccatcttgc 180
tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa acatctgaag 240
agctagtcta tcagcatctg acaggtgaat tggatggttc tcagaaccat ttcacccaga 300
cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca taacaaaccc 360
tgctccaatc tgtcacataa aagtctgtga cttgaagttt agtcagcacc cccaccaaac 420
tttattttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataaag tacccatgtc 480
ttta 484

<210> 435
<211> 424
<212> DNA
<213> Homo sapiens

<400> 435
gcgccgctca gagcaggtca ctttctgcct tccacgtcct ccttcaagga agccccatgt 60
gggtagcttt caatatcgca ggttcttact cctctgcctc tataagctca aacccaccaa 120
cgatcgggca agtaaacccc ctccctcgcc gacttcggaa ctggcgagag ttcagcgcag 180
atgggcctgt ggggaggggg caagatagat gagggggagc ggcatggtgc ggggtgaccc 240
cttggagaga ggaaaaaggc cacaagaggg gctgccaccg ccactaacgg agatggccct 300
ggtagagacc tttgggggtc tggaacctct ggactcccca tgctctaact cccacactct 360
gctatcagaa acttaaactt gaggattttc tctgtttttc actcgcaata aattcagagc 420
aaac 424

<210> 436
<211> 667
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(667)
<223> n = A,T,C or G

<400> 436
accttgggaa nactctcaca atataaaggg tcgtagactt tactccaaat tccaaaaagg 60
tcctggccat gtaatcctga aagttttccc aaggtagcta taaaatcctt ataagggtgc 120
agcctcttct ggaattcctc tgatttcaaa gtctcactct caagttcttg aaaacgaggg 180
cagttcctga aaggcaggta tagcaactga tcttcagaaa gaggaactgt gtgcaccggg 240
atgggctgcc agagtaggat aggattccag atgctgacac cttctggggg aaacagggct 300
gccaggtttg tcatagcact catcaaagtc cggtcaacgt ctgtgcttcg aatataaacc 360

```
tgttcatgtt tataggactc attcaagaat tttctatatc tctttcttat atactctcca 420
agttcataat gctgctccat gcccagctgg gtgagttggc caaatccttg tggccatgag 480
gattccttta tggggtcagt gggaaaggtg tcaatgggac ttcggtctcc atgccgaaac 540
accaaagtca caaacttcaa ctccttggct agtacacttc ggtctagcca gaaaaaaagc 600
agaaacaaga agccaaggct aaggcttgct gccctgccag gaggaggggt gcagctctca 660
tgttgag                                                         667
```

<210> 437
<211> 693
<212> DNA
<213> Homo sapiens

<400> 437
```
ctacgtctca accctcattt ttaggtaagg aatcttaagt ccaaagatat taagtgactc 60
acacagccag gtaaggaaag ctggattggc acactaggac tctaccatac cgggttttgt 120
taaagctcag gttaggaggc tgataagctt ggaaggaact tcagacagct ttttcagatc 180
ataaaagata attcttagcc catgttcttc tccagagcag acctgaaatg acagcacagc 240
aggtactcct ctattttcac ccctcttgct tctactctct ggcagtcaga cctgtgggag 300
gccatgggag aaagcagctc tctggatgtt tgtacagatc atggactatt ctctgtggac 360
catttctcca ggttacccta ggtgtcacta ttgggggggac agccagcatc tttagctttc 420
atttgagttt ctgtctgtct tcagtagagg aaactttttgc tcttcacact tcacatctga 480
acacctaact gctgttgctc ctgaggtggt gaaagacaga tatagagctt acagtattta 540
tcctatttct aggcactgag ggctgtgggg taccttgtgg tgccaaaaca gatcctgttt 600
taaggacatg ttgcttcaga gatgtctgta actatctggg ggctctgttg gctctttacc 660
ctgcatcatg tgctctcttg gctgaaaatg acc                            693
```

<210> 438
<211> 360
<212> DNA
<213> Homo sapiens

<400> 438
```
ctgcttatca caatgaatgt tctcctgggc agcgttgtga tctttgccac cttcgtgact 60
ttatgcaatg catcatgcta tttcatacct aatgagggag ttccaggaga ttcaaccagg 120
atgtttctac acctgtgggt tatgacaaag acaactgcca aagaatcttc aagaaggagg 180
actgcaagta tatctggtgg agaagaagga cccaaaaaag acctgttctg tcagtgaatg 240
gataatctaa tgtgcttcta gtaggcacag ggctcccagg ccaggcctca ttctcctctg 300
gcctctaata gtcaataatt gtgtagccat gcctatcagt aaaaagattt ttgagcaaac 360
```

<210> 439
<211> 431
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(431)
<223> n = A,T,C or G

<400> 439
```
gttcctnnta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gcttttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag t                                                    431
```

150

```
<210> 440
<211> 523
<212> DNA
<213> Homo sapiens

<400> 440
agagataaag cttaggtcaa agttcataga gttcccatga actatatgac tggccacaca 60
ggatctttg  tatttaagga ttctgagatt ttgcttgagc aggattagat aaggctgttc 120
tttaaatgtc tgaaatggaa cagatttcaa aaaaaaaccc cacaatctag ggtgggaaca 180
aggaaggaaa gatgtgaata ggctgatggg caaaaaacca atttacccat cagttccagc 240
cttctctcaa ggagaggcaa agaaaggaga tacagtggag acatctggaa agttttctcc 300
actggaaaac tgctactatc tgtttttata tttctgttaa aatatatgag gctacagaac 360
taaaaattaa aacctctttg tgtcccttgg tcctggaaca tttatgttcc ttttaaagaa 420
acaaaaatca aactttacag aaagatttga tgtatgtaat acatatagca gctcttgaag 480
tatatatatc atagcaaata agtcatctga tgagaacaag cta                    523

<210> 441
<211> 430
<212> DNA
<213> Homo sapiens

<400> 441
gttcctccta actcctgcca gaaacagctc tcctcaacat gagagctgca cccctcctcc 60
tggccagggc agcaagcctt agccttggct tcttgtttct gctttttttc tggctagacc 120
gaagtgtact agccaaggag ttgaagtttg tgactttggt gtttcggcat ggagaccgaa 180
gtcccattga cacctttccc actgacccca taaaggaatc ctcatggcca caaggatttg 240
gccaactcac ccagctgggc atggagcagc attatgaact tggagagtat ataagaaaga 300
gatatagaaa attcttgaat gagtcctata aacatgaaca ggtttatatt cgaagcacag 360
acgttgaccg gactttgatg agtgctatga caaacctggc agcccgtcga cgcggccgcg 420
aatttagtag                                                         430

<210> 442
<211> 362
<212> DNA
<213> Homo sapiens

<400> 442
ctaaggaatt agtagtgttc ccatcacttg tttggagtgt gctattctaa aagattttga 60
tttcctggaa tgacaattat attttaactt tggtggggga aagagttata ggaccacagt 120
cttcacttct gatacttgta aattaatctt ttattgcact tgtttttgacc attaagctat 180
atgtttagaa atggtcattt tacggaaaaa ttagaaaaat tctgataata gtgcagaata 240
aatgaattaa tgttttactt aatttatatt gaactgtcaa tgacaaataa aaattctttt 300
tgattatttt ttgttttcat ttaccagaat aaaaactaag aattaaaagt ttgattacag 360
tc                                                                 362

<210> 443
<211> 624
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(624)
<223> n = A,T,C or G

<400> 443
tttttttttt gcaacacaat atacatcaca gtgaaatgtg taatccttgc aaattgcaag 60
```

```
ttgaaagaat taaattcaga ggaggggaga gaaagagtac tcagtaggga ctgagcacta 120
aatgcttatt ttaaaagaaa tgtaaagagc agaaagcaat tcaggctacc ctgcctttttg 180
tgctggctag tactccggtc ggtgtcagca gcacgtggca ttgaacattg caatgtggag 240
cccaaaccac agaaaatggg gtgaaattgg ccaactttct attaacttgg cttcctgttt 300
tataaaatat tgtgaataat atcacctact tcaaagggca gttatgaggc ttaaatgaac 360
taacgcctac aaaacactta aacatagata acataggtgc aagtactatg tatctggtac 420
atggtaaaca tccttattat taaagtcaac gctaaaatga atgtgtgtgc atatgctaat 480
agtacagaga gagggcactt aaaccaacta agggcctgga gggaaggttt cctggaaaga 540
ngatgcttgt gctgggtcca aatcttggtc tactatgacc ttggccaaat tatttaaact 600
ttgtccctat ctgctaaaca gatc                                       624
```

```
<210> 444
<211> 425
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(425)
<223> n = A,T,C or G

<400> 444
gcacatcatt nntcttgcat tctttgagaa taagaagatc agtaaatagt tcagaagtgg 60
gaagctttgt ccaggcctgt gtgtgaaccc aatgttttgc ttagaaatag aacaagtaag 120
ttcattgcta tagcataaca caaaatttgc ataagtggtg gtcagcaaat ccttgaatgc 180
tgcttaatgt gagaggttgg taaaatcctt tgtgcaacac tctaactccc tgaatgtttt 240
gctgtgctgg gacctgtgca tgccagacaa ggccaagctg ctgaaagag caaccagcca 300
cctctgcaat ctgccacctc ctgctggcag gatttgtttt tgcatcctgt gaagagccaa 360
ggaggcacca gggcataagt gagtagactt atggtcgacg cggccgcgaa tttagtagta 420
gtaga                                                            425
```

```
<210> 445
<211> 414
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

<400> 445
catgtttatg nttttggatt actttgggca cctagtgttt ctaaatcgtc tatcattctt 60
ttctgttttt caaaagcaga gatggccaga gtctcaacaa actgtatctt caagtctttg 120
tgaaattctt tgcatgtggc agattattgg atgtagtttc ctttaactag catataaatc 180
tggtgtgttt cagataaatg aacagcaaaa tgtggtggaa ttaccatttg gaacattgtg 240
aatgaaaaat tgtgtctcta gattatgtaa caaataacta tttcctaacc attgatcttt 300
ggattttttat aatcctactc acaaatgact aggcttctcc tcttgtattt tgaagcagtg 360
tgggtgctgg attgataaaa aaaaaaaaag tcgacgcggc cgcgaattta gtag       414
```

```
<210> 446
<211> 631
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(631)
```

```
<223> n = A,T,C or G

<400> 446
acaaattaga anaaagtgcc agagaacacc acataccttg tccggaacat tacaatggct 60
tctgcatgca tgggaagtgt gagcattcta tcaatatgca ggagccatct tgcaggtgtg 120
atgctggtta tactggacaa cactgtgaaa aaaaggacta cagtgttcta tacgttgttc 180
ccggtcctgt acgatttcag tatgtcttaa tcgcagctgt gattggaaca attcagattg 240
ctgtcatctg tgtggtggtc ctctgcatca caagggccaa actttaggta atagcattgg 300
actgagattt gtaaactttc caaccttcca ggaaatgccc cagaagcaac agaattcaca 360
gacagaagca aaatacaggg cactacagtt cagacaatac aacaagagcg tccacgaggt 420
taatctaaag ggagcatgtt tcacagtggc tggactaccg agagcttgga ctacacaata 480
cagtattata gacaaaagaa taagacaaga gatctacaca tgttgccttg catttgtggt 540
aatctacacc aatgaaaaca tgtactacag ctatatttga ttatgtatgg atatatttga 600
aatagtatac attgtcttga tgttttttct g                                631

<210> 447
<211> 585
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(585)
<223> n = A,T,C or G

<400> 447
ccttgggaaa antntcacaa tataaagggt cgtagacttt actccaaatt ccaaaaaggt 60
cctggccatg taatcctgaa agttttccca aggtagctat aaaatcctta taagggtgca 120
gcctcttctg gaattcctct gatttcaaag tctcactctc aagttcttga aaacgagggc 180
agttcctgaa aggcaggtat agcaactgat cttcagaaag aggaactgtg tgcaccggga 240
tgggctgcca gagtaggata ggattccaga tgctgacacc ttctggggga aacagggctg 300
ccaggtttgt catagcactc atcaaagtcc ggtcaacgtc tgtgcttcga atataaacct 360
gttcatgttt ataggactca ttcaagaatt ttctatatct ctttcttata tactctccaa 420
gttcataatg ctgctccatg cccagctggg tgagttggcc aaatccttgt ggccatgagg 480
attcctttat ggggtcagtg ggaaaggtgt caatgggact tcggtctcca tgccgaaaca 540
ccaaagtcac aaacttcaac tccttggcta gtacacttcg gtcta             585

<210> 448
<211> 93
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(93)
<223> n = A,T,C or G

<400> 448
tgctcgtggg tcattctgan nnccgaactg accntgccag ccctgccgan gggccnccat 60
ggctccctag tgccctggag agganggggc tag                           93

<210> 449
<211> 706
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
```

<222> (1)...(706)
<223> n = A,T,C or G

<400> 449
ccaagttcat gctntgtgct ggacgctgga cagggggcaa aagcnnttgc tcgtgggtca 60
ttctgancac cgaactgacc atgccagccc tgccgatggt cctccatggc tccctagtgc 120
cctggagagg aggtgtctag tcagagagta gtcctggaag gtggcctctg ngaggagcca 180
cggggacagc atcctgcaga tggtcgggcg cgtcccattc gccattcagg ctgcgcaact 240
gttgggaagg gcgatcggtg cgggcctctt cgctattacg ccagctggcg aaaggggggat 300
gtgctgcaag gcgattaagt tgggtaacgc caggggttttc ccagtcncga cgttgtaaaa 360
cgacggccag tgaattgaat ttaggtgacn ctatagaaga gctatgacgt cgcatgcacg 420
cgtacgtaag cttggatcct ctagagcggc cgcctactac tactaaattc gcggccgcgt 480
cgacgtggga tccncactga gagagtggag agtgacatgt gctggacnct gtccatgaag 540
cactgagcag aagctggagg cacaacgcnc cagacactca cagctactca ggaggctgag 600
aacaggttga acctgggagg tggaggttgc aatgagctga gatcaggccn ctgcnccca 660
gcatggatga cagagtgaaa ctccatctta aaaaaaaaa aaaaaa   706

<210> 450
<211> 493
<212> DNA
<213> Homo sapiens

<400> 450
gagacggagt gtcactctgt tgcccaggct ggagtgcagc aagacactgt ctaagaaaaa 60
acagttttaa aaggtaaaac aacataaaaa gaaatatcct atagtggaaa taagagagtc 120
aaatgaggct gagaacttta caaagggatc ttacagacat gtcgccaata tcactgcatg 180
agcctaagta taagaacaac ctttggggag aaaccatcat ttgacagtga ggtacaattc 240
caagtcaggt agtgaaatgg gtggaattaa actcaaatta atcctgccag ctgaaacgca 300
agagacactg tcagagagtt aaaaagtgag ttctatccat gaggtgattc cacagtcttc 360
tcaagtcaac atctgtga actcacagac caagttctta aaccactgtt caaactctgc 420
tacacatcag aatcacctgg agagctttac aaactcccat tgccgagggt cgacgcggcc 480
gcgaatttag tag   493

<210> 451
<211> 501
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(501)
<223> n = A,T,C or G

<400> 451
gggcgcgtcc cattcgccat tcaggctgcg caactgttgg gaagggcgat cggtgcgggc 60
ctcttcgcta ttacgccagc tggcgaaagg gggatgtgct gcaaggcgat taagttgggt 120
aacgccaggg ttttcccagt cncgacgttg taaaacgacg gccagtgaat tgaatttagg 180
tgacnctata gaagagctat gacgtcgcat gcacgcgtac gtaagcttgg atcctctaga 240
gcggccgcct actactacta aattcgcggc cgcgtcgacg tgggatccnc actgagagag 300
tggagagtga catgtgctgg acnctgtcca tgaagcactg agcagaagct ggaggcacaa 360
cgcnccagac actcacagct actcaggagg ctgagaacag gttgaacctg ggaggtggag 420
gttgcaatga gctgagatca ggccnctgcn ccccagcatg gatgacagag tgaaactcca 480
tcttaaaaaa aaaaaaaaa a   501

<210> 452
<211> 51
<212> DNA
<213> Homo sapiens

```
<220>
<221> misc_feature
<222> (1)...(51)
<223> n = A,T,C or G

<400> 452
agacggtttc accnttacaa cnccttttag gatgggnntt ggggagcaag c          51


<210> 453
<211> 317
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(317)
<223> n = A,T,C or G

<400> 453
tacatcttgc tttttcccca ttggaactag tcattaaccc atctctgaac tggtagaaaa 60
acatctgaag agctagtcta tcagcatctg gcaagtgaat tggatggttc tcagaaccat 120
ttcacccana cagcctgttt ctatcctgtt taataaatta gtttgggttc tctacatgca 180
taacaaaccc tgctccaatc tgtcacataa aagtctgtga cttgaagttt antcagcacc 240
cccaccaaac tttatttttc tatgtgtttt ttgcaacata tgagtgtttt gaaaataagg 300
tacccatgtc tttatta                                                 317


<210> 454
<211> 231
<212> DNA
<213> Homo sapiens

<400> 454
ttcgaggtac aatcaactct cagagtgtag tttccttcta tagatgagtc agcattaata 60
taagccacgc cacgctcttg aaggagtctt gaattctcct ctgctcactc agtagaacca 120
agaagaccaa attcttctgc atcccagctt gcaaacaaaa ttgttcttct aggtctccac 180
ccttcctttt tcagtgttcc aaagctcctc acaatttcat gaacaacagc t           231


<210> 455
<211> 231
<212> DNA
<213> Homo sapiens

<400> 455
taccaaagag ggcataataa tcagtctcac agtagggttc accatcctcc aagtgaaaaa 60
cattgttccg aatgggcttt ccacaggcta cacacacaaa acaggaaaca tgccaagttt 120
gtttcaacgc attgatgact tctccaagga tcttcctttg gcatcgacca cattcagggg 180
caaagaattt ctcatagcac agctcacaat acagggctcc tttctcctct a           231


<210> 456
<211> 231
<212> DNA
<213> Homo sapiens

<400> 456
ttggcaggta cccttacaaa gaagacacca taccttatgc gttattaggt ggaataatca 60
ttccattcag tattatcgtt attattcttg gagaaaccct gtctgtttac tgtaaccttt 120
tgcactcaaa ttcctttatc aggaataact acatagccac tatttacaaa gccattggaa 180
```

```
ccttttttatt tggtgcagct gctagtcagt ccctgactga cattgccaag t          231
```

<210> 457
<211> 231
<212> DNA
<213> Homo sapiens

<220>
<221> misc_feature
<222> (1)...(231)
<223> n = A,T,C or G

<400> 457
```
cgaggtaccc aggggtctga aaatctctnn tttantagtc gatagcaaaa ttgttcatca 60
gcattcctta atatgatctt gctataatta gattttttctc cattagagtt catacagttt 120
tatttgattt tattagcaat ctctttcaga agacccttga gatcattaag ctttgtatcc 180
agttgtctaa atcgatgcct catttcctct gaggtgtcgc tggctttttgt g          231
```

<210> 458
<211> 231
<212> DNA
<213> Homo sapiens

<400> 458
```
aggtctggtt cccccactt ccactcccct ctactctctc taggactggg ctgggccaag 60
agaagagggg tggttaggga agccgttgag acctgaagcc ccaccctcta ccttccttca 120
acaccctaac cttgggtaac agcatttgga attatcattt gggatgagta gaatttccaa 180
ggtcctgggt taggcatttt gggggggccag accccaggag aagaagattc t          231
```

<210> 459
<211> 231
<212> DNA
<213> Homo sapiens

<400> 459
```
ggtaccgagg ctcgctgaca cagagaaacc ccaacgcgag gaaaggaatg gccagccaca 60
ccttcgcgaa acctgtggtg gcccaccagt cctaacggga caggacagag agacagagca 120
gccctgcact gttttccctc caccacagcc atcctgtccc tcattggctc tgtgctttcc 180
actatacaca gtcaccgtcc caatgagaaa caagaaggag caccctccac a          231
```

<210> 460
<211> 231
<212> DNA
<213> Homo sapiens

<400> 460
```
gcaggtataa catgctgcaa caacagatgt gactaggaac ggccggtgac atggggaggg 60
cctatcaccc tattcttggg ggctgcttct tcacagtgat catgaagcct agcagcaaat 120
cccacctccc cacacgcaca cggccagcct ggagcccaca gaagggtcct cctgcagcca 180
gtggagcttg gtccagcctc cagtccaccc ctaccaggct taaggataga a          231
```

<210> 461
<211> 231
<212> DNA
<213> Homo sapiens

<400> 461
```
cgaggtttga gaagctctaa tgtgcagggg agccgagaag caggcggcct agggagggtc 60
```

```
gcgtgtgctc cagaagagtg tgtgcatgcc agaggggaaa caggcgcctg tgtgtcctgg 120
gtggggttca gtgaggagtg ggaaattggt tcagcagaac caagccgttg ggtgaataag 180
aggggattc catggcactg atagagccct atagtttcag agctgggaat t          231


<210> 462
<211> 231
<212> DNA
<213> Homo sapiens


<400> 462
aggtaccctc attgtagcca tgggaaaatt gatgttcagt ggggatcagt gaattaaatg 60
gggtcatgca agtataaaaa ttaaaaaaaa aagacttcat gcccaatctc atatgatgtg 120
gaagaactgt tagagagacc aacagggtag tgggttagag atttccagag tcttacattt 180
tctagaggag gtatttaatt tcttctcact catccagtgt tgtatttagg a          231


<210> 463
<211> 231
<212> DNA
<213> Homo sapiens


<400> 463
tactccagcc tggtgacaga gcgagaccct atcaccgccc cccaccccac caaaaaaaaa 60
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catttgacag gtgtcttttc ctctggacct cggtgtcccc atctgagtga gaaaaggcag 180
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<210> 464
<211> 231
<212> DNA
<213> Homo sapiens


<400> 464
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cctgcttcag tgactgtgtg cctgtagtcc cagctactcg ggagtctgtg tgaggccagg 180
ggtgccagcg caccagctag atgctctgta acttctaggc cccattttcc c          231


<210> 465
<211> 231
<212> DNA
<213> Homo sapiens


<400> 465
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aggatggcac aatttttgct tgtgttcata atatactcag attagttcag ctccatcaga 180
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<210> 466
<211> 231
<212> DNA
<213> Homo sapiens


<400> 466
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cctgtgcaat caaatattgt ggagaattcc ctagctggag aagtcacaaa gactataggc 180
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<211> 311
<212> DNA
<213> Homo sapiens

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tgtgccttaa cagaaggtct tgagattcta agtgggaatc atttcagtga ctgtcatgtg 180
gcatgggtct ctgcccaagc tcgtaatgag actatagcaa ggcggctgtg ggacgtcagt 240
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ctgcagcaga c   311

<210> 468
<211> 3112
<212> DNA
<213> Homo sapiens

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tggaaggcac tggatgcctg atgatgaagt ggactttcaa actgggcac tactgaaacg 180
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<210> 469
<211> 2229
<212> DNA
<213> Homo sapiens

<400> 469
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tgatttgcca aaattctaaa gcgcactcac catgaaatgg ataaaggtta cctttgggga 180
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<211> 2426
<212> DNA
<213> Homo sapiens

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caaaattcta aagcgcactc accatgaaat ggataaaggt taccttttggg gatttgcact 180
gcatgaattc tgtgaaaagc ttgttggata ttgtgataga gatagagaaa tgaagtatat 240
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<210> 471
<211> 812
<212> DNA
<213> Homo sapiens

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aaatattaaa aatgagtgtg gctggatata tggagaatgt tgggcccaga aggaaccgta 120
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<210> 472
<211> 515
<212> DNA
<213> Homo sapiens

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<223> n = A,T,C or G

<400> 472
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gttccagaat tattggtcct tgcagcccgg tgaatctcag caagaggaac caccaactga 180
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<211> 5829
<212> DNA
<213> Homo sapiens

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<212> DNA
<213> Homo sapiens

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<210> 475
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163

<211> 2414
<212> DNA
<213> Homo sapiens

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<222> (33)
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<211> 3434
<212> DNA
<213> Homo sapiens

<400> 476

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<211> 140
<212> PRT
<213> Homo sapiens

<400> 477
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His Tyr His Arg Asp Thr Asp Thr Arg Arg His His His Met Asp Thr
                 20   25   30

Leu Ser His Tyr His Arg Asp Thr Arg His His Thr Val Thr Trp Thr
             35   40   45

His His His Thr His Glu His Thr Asp Thr Leu Pro Tyr Gly His Trp
         50   55   60

His Thr His Cys His Thr Val Thr Trp Thr His Leu His Thr Ile Thr
65   70   75   80

Pro Pro His Thr Leu Pro Val Asp Thr Arg Thr His Arg His Cys His
                 85   90   95

Thr Asp Thr Gln Asn Thr Val Thr Arg Arg His His His Ala Asp Thr
                100   105   110

Pro Pro Leu Trp Cys Arg Leu Asn Tyr Pro Ala Gly Gly Thr Ala Val
             115   120   125

Ala Tyr Ser Cys Leu Ser Asp Trp Leu Ser Pro Gln
         130   135   140

<210> 478
<211> 143
<212> PRT
<213> Homo sapiens

<400> 478
Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
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Ser His Gly His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
                 20   25   30

Gly Glu Ile Thr Trp Thr His His His Thr Ile Thr Gly Thr Gln Thr
             35   40   45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
         50   55   60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65   70   75   80

Pro Thr His Cys His Met Asp Thr Gly Thr His Thr Ala Thr Leu Ser
                 85   90   95

```
His Gly His Thr Ser Thr Pro Ser His His His Thr His Cys Leu Trp
            100             105             110

Thr Gln Gly His Thr Asp Thr Val Thr Gln Ile His Lys Thr Leu Ser
            115             120             125

His Gly Asp Ile Thr Met Gln Ile His His His Ser Gly Ala Val
    130             135             140
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<210> 479
<211> 222
<212> PRT
<213> Homo sapiens

<400> 479
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Met Tyr Arg His Thr Glu Thr Leu Pro His Gly Asp Thr Val Thr Gln
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Ser His Glu His Thr Gly Ile Val Thr Trp Thr Asp Thr Gln Thr Tyr
            20              25              30

Gly Glu Ile Thr Leu Thr His His His Thr Ile Thr Gly Thr Gln Thr
            35              40              45

His Gly Asp Ile Thr Thr Trp Thr His Cys His Thr Thr Thr Gly Thr
    50              55              60

Arg Asp Ile Thr Leu Ser His Gly His Thr Ile Thr His Met Asn Thr
65              70              75              80

Pro Thr His Cys His Met Asp Thr Ala Thr His Thr Ala Thr Leu Ser
                85              90              95

His Gly His Thr Ser Ile Pro Ser His His His Thr His Cys His Val
            100             105             110

Asp Thr Arg Thr His Arg His Cys His Thr Asp Thr Gln Asn Thr Val
            115             120             125

Thr Arg Arg His His His Ala Asp Thr Pro Pro His Gly His Ser Thr
    130             135             140

Arg His Ser Ala Thr Gln Ile His His His Thr Glu Met Arg Thr His
145             150             155             160

Cys His Thr Asp Thr Thr Thr Ser Leu Pro His Phe His Val Ser Ala
                165             170             175

Gly Gly Val Gly Pro Thr Thr Leu Gly Ser Asn Arg Glu Ile Thr Trp
            180             185             190

Thr Tyr Ser Glu Gly Lys Ile Phe Phe Tyr Phe Leu Gly Asn Gln Ala
            195             200             205

Arg Leu Cys Leu Lys Lys Arg Lys Lys Lys Gln Tyr Thr Val
    210             215             220
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<210> 480
<211> 144
<212> PRT
<213> Homo sapiens

<400> 480
Met Glu Pro Tyr Arg Gly Asn Glu Gln Pro Ser Gln Glu Gln Gly Val
                    5   10   15

Cys Cys Leu Trp Gly Leu Gln Ser Leu Pro Gln Gly Ser Tyr Val Thr
                20   25   30

Val Gly Phe Leu Val Val Lys Arg Gln Thr Ile Gly Arg Leu Glu Arg
            35   40   45

Asp Phe Met Phe Lys Cys Arg Lys Gln Pro Gly Leu Pro Pro Ser Gly
        50   55   60

Leu Cys Leu Leu Trp Pro Trp Pro Asn Leu Glu Phe Gly Arg Arg Gln
65   70   75   80

Asp Arg Leu Thr Trp Ser Ser Val Ser Val Ala Gly Val Cys Ala Cys
                85   90   95

Arg Ala Arg Pro Gly Trp Leu Gly Glu Gln Pro Ala Thr Ser Ala Gly
                100   105   110

Val Arg Leu Glu Gln Val Glu Gln Pro Pro Ala His Pro Leu Gln Glu
            115   120   125

Ala Gly Val Ala Arg Phe Pro Arg Pro Glu Trp Val Pro Pro Asn Gly
        130   135   140

<210> 481
<211> 167
<212> PRT
<213> Homo sapiens

<400> 481
Met His Gly Pro Gln Val Leu Ala Arg Cys Ser Glu Cys Ala Cys Pro
                5   10   15

Ala Leu Ala Ala Thr Ser Ala Gly Val Arg Leu Glu Gly Val Asp Arg
                20   25   30

Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys Ser His Ser
            35   40   45

Leu Ser Gly Cys His Leu Met Ala Asp Gly Ala Lys Ala Leu Gly Lys
        50   55   60

Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr Asp Val Pro

```
            65                    70                    75                    80
       Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser Ser Trp Arg
                        85                    90                    95

       Ala Leu Ala Glu Val Thr Gly Cys Ser Leu Gly Pro Leu Gly Leu Ala
                       100                   105                   110

       Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys Trp Ser His
                       115                   120                   125

       Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr Ala Ala Phe
                       130                   135                   140

       Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu Trp Ala Ser
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       Trp Leu Ser Arg Gly Arg Pro
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       <210> 482
       <211> 143
       <212> PRT
       <213> Homo sapiens

       <400> 482
       Met Glu Pro Tyr Arg Gly Asn Lys Lys Gln Val Gln Glu Lys Gly Val
                         5                    10                    15

       Pro Cys Leu Trp Gly Ser Ser Pro Cys Leu Arg Cys His Met Ala Leu
                        20                    25                    30

       Arg Ala Ser Trp Leu Pro Gly Gly Gly Pro Gln Ala Ile Leu Gly Arg
                        35                    40                    45

       Thr Leu Cys Ser Ser Ala Glu Ser Ser Gln Asp Cys His Pro Gly Gly
                50                    55                    60

       Pro Ser Ile Ala Leu Ala Lys Pro Cys Arg Gly Val Trp Leu Leu Phe
       65                    70                    75                    80

       Glu Pro Ala Trp Pro Pro Trp His Ala Arg Ala Pro Gly Ala Gly Thr
                        85                    90                    95

       Leu Leu Arg Val Cys Leu Ser Cys Leu Gly Cys His Leu Cys Gly Gly
                       100                   105                   110

       Ala Ser Gly Gly Gly Gly Pro Ala Thr Asn Leu Thr Gln Ser Arg Lys
                       115                   120                   125

       Trp Met Ala Met Phe Pro Gln Pro Glu Trp Leu Pro Pro Asp Gly
                       130                   135                   140


       <210> 483
       <211> 143
       <212> PRT
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<213> Homo sapiens

<400> 483
Met Gln Thr Gln Arg Gly Asn Lys Gln Arg Ala Gln Glu Gln Gly Val
                  5   10   15

Cys Cys Leu Trp Gly Ser Ser Pro Cys Leu Gly Ser Tyr Gly Thr Ala
              20   25   30

Gly Phe Leu Val Ala Lys Arg Arg Thr Thr Gly Leu Leu Glu Glu Asp
          35   40   45

Phe Thr Phe Lys Cys Arg Lys Gln Pro Lys Leu Pro Ser Met Arg Leu
      50   55   60

Ser Leu Leu Trp Pro Trp Arg Asp Leu Lys Phe Val Pro Arg Gln Asp
65   70   75   80

Lys Leu Thr Arg Ser Ser Val Ser Val Ala Gly Ala Tyr Ala Cys Arg
                  85   90   95

Ala Gly Pro Gly Trp Leu Lys Glu Gln Pro Ala Thr Ser Ala Arg Val
              100   105   110

Arg Leu Val Gln Ala Glu His Pro Pro Pro His Pro Leu Glu Glu Val
          115   120   125

Gly Met Ala Arg Phe Pro Gln Pro Glu Cys Leu Pro Pro Tyr Cys
      130   135   140

        <210> 484
        <211> 30
        <212> PRT
        <213> Homo Sapien

        <400> 484
Thr Ala Ala Ser Asp Asn Phe Gln Leu Ser Gln Gly Gly Gln Gly Phe
1   5   10   15
Ala Ile Pro Ile Gly Gln Ala Met Ala Ile Ala Gly Gln Ile
              20   25   30

        <210> 485
        <211> 31
        <212> DNA
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 485
gggaagctta tcacctatgt gccgcctctg c   31

        <210> 486
        <211> 27
        <212> DNA
        <213> Artificial Sequence

        <220>

<223> Made in a lab

<400> 486
gcgaattctc acgctgagta tttggcc   27

        <210> 487
        <211> 36
        <212> DNA
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 487
cccgaattct tagctgccca tccgaacgcc ttcatc   36

        <210> 488
        <211> 33
        <212> DNA
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 488
gggaagcttc ttccccggct gcaccagctg tgc   33

        <210> 489
        <211> 19
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 489
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
1   5   10   15
Ser Val Ala

        <210> 490
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 490
Tyr Leu Ala Ser Val Ala Ala Phe Pro Val Ala Ala Gly Ala Thr Cys
1   5   10   15
Leu Ser His Ser
            20

        <210> 491
        <211> 20
        <212> PRT

<210> Artificial Sequence

<220>
<223> Made in a lab

<400> 491
Thr Cys Leu Ser His Ser Val Ala Val Val Thr Ala Ser Ala Ala Leu
1   5   10   15
Thr Gly Phe Thr
            20

<210> 492
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 492
Ala Leu Thr Gly Phe Thr Phe Ser Ala Leu Gln Ile Leu Pro Tyr Thr
1   5   10   15
Leu Ala Ser Leu
            20

<210> 493
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 493
Tyr Thr Leu Ala Ser Leu Tyr His Arg Glu Lys Gln Val Phe Leu Pro
1   5   10   15
Lys Tyr Arg Gly
            20

<210> 494
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 494
Leu Pro Lys Tyr Arg Gly Asp Thr Gly Gly Ala Ser Ser Glu Asp Ser
1   5   10   15
Leu Met Ile Ser
            20

<210> 495
<211> 20
<212> PRT
<213> Artificial Sequence

```
        <220>
        <223> Made in a lab


        <400> 495
Asp Ser Leu Met Thr Ser Phe Leu Pro Gly Pro Lys Pro Gly Ala Pro
1               5                   10                  15
Phe Pro Asn Gly
            20


        <210> 496
        <211> 21
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab


        <400> 496
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1               5                   10                  15
Pro Pro Pro Pro Ala
            20


        <210> 497
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab


        <400> 497
Leu Leu Pro Pro Pro Pro Ala Leu Cys Gly Ala Ser Ala Cys Asp Val
1               5                   10                  15
Ser Val Arg Val
            20


        <210> 498
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab


        <400> 498
Asp Val Ser Val Arg Val Val Val Gly Glu Pro Thr Glu Ala Arg Val
1               5                   10                  15
Val Pro Gly Arg
            20


        <210> 499
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
```

<223> Made in a lab

<400> 499
Arg Val Val Pro Gly Arg Gly Ile Cys Leu Asp Leu Ala Ile Leu Asp
1   5   10   15
Ser Ala Phe Leu
            20

<210> 500
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 500
Leu Asp Ser Ala Phe Leu Leu Ser Gln Val Ala Pro Ser Leu Phe Met
1   5   10   15
Gly Ser Ile Val
            20

<210> 501
<211> 20
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 501
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val Thr Ala Tyr Met
1   5   10   15
Val Ser Ala Ala
            20

<210> 502
<211> 414
<212> DNA
<213> Homo Sapien

<220>
<221> misc_feature
<222> (1)...(414)
<223> n = A,T,C or G

<400> 502
caccatggag acaggcctgc gctggctttt cctggtcgct gtgctcaaag gtgtccaatg   60
tcagtcggtg gaggagtccg ggggtcgcct ggtcacgcct gggacacctt tgacantcac   120
ctgtagagtt tttggaatng acctcagtag caatgcaatg agctgggtcc gccaggctcc   180
agggaagggg ctggaatgga tcggagccat tgataattgt ccacantacg cgacctgggc   240
gaaaggccga ttnatnattt ccaaaacctn gaccacggtg gatttgaaaa tgaccagtcc   300
gacaaccgag gacacggcca cctattttg tggcagaatg aatactggta atagtggttg   360
gaagaatatt tggggcccag gcaccctggt caccgtntcc tcagggcaac ctaa   414

<210> 503
<211> 379
<212> DNA

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        <213> Homo Sapiens

        <220>
        <221> misc_feature
        <222> (1)...(379)
        <223> n = A,T,C or G

        <400> 503
atncgatggt gcttggtcaa aggtgtccag tgtcagtcgg tggaggagtc cgggggtcgc          60
ctggtcacgc ctgggacacc cctgacactc acctgcaccg tntctggatt ngacatcagt         120
agctatggag tgagctgggt ccgccaggct ccagggaagg ggctggnata catcggatca         180
ttagtagtag tggtacattt tacgcgagct gggcgaaagg ccgattcacc atttccaaaa         240
cctngaccac ggtggatttg aaaatcacca gtttgacaac cgaggacacg gccacctatt         300
tntgtgccag aggggggttt aattataaag acatttgggg cccaggcacc ctggtcaccg         360
tntccttagg gcaacctaa                                                       379

        <210> 504
        <211> 19
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 504
Gly Phe Thr Asn Tyr Thr Asp Phe Glu Asp Ser Pro Tyr Phe Lys Glu
1               5                   10                  15
Asn Ser Ala

        <210> 505
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 505
Lys Glu Asn Ser Ala Phe Pro Pro Phe Cys Cys Asn Asp Asn Val Thr
1               5                   10                  15
Asn Thr Ala Asn
            20

        <210> 506
        <211> 407
        <212> DNA
        <213> Homo Sapien

        <400> 506
atggagacag gcctgcgctg gcttctcctg gtcgctgcgc tcaaaggtgt ccagtgtcag          60
tcgctggagg agtccggggg tcgcctggtc acgcctggga cacccctgac actcacctgc         120
accgtctctg gattctccct cagtagcaat gcaatgatct gggtccgcca ggctccaggg         180
aaggggctgg aatacatcgg atacattagt tatggtggta gcgcatacta cgcgagctgg         240
gtgaaaggcc gattcaccat ctccaaaacc tcgaccacgg tggatctgag aatgaccagt         300
ctgacaaccg aggacacggc cacctatttc tgtgccagaa atagtgattt tagtggtatg         360
ttgtggggcc aggcaccct ggtcaccgtc tcctcagggc aacctaa                        407
```

```
<210> 507
<211> 422
<212> DNA
<213> Homo Sapien

<400> 507
atggagacag gcctgcgctg gcttctcctg gtcgctgtgc tcaaaggtgt ccagtgtcag    60
tcggtggagg agtccggggg tcgcctggtc acgcctggga cacccctgac actcacctgt   120
acagtctctg gattctccct cagcaactac gacctgaact gggtccgcca ggctccaggg   180
aagggctgg  aatggatcgg gatcattaat tatgttggta ggacggacta cgcgaactgg   240
gcaaaaggcc ggttcaccat ctccaaaacc tcgaccaccg tggatctcaa gatcgccagt   300
ccgacaaccg aggacacggc cacctatttc tgtgccagag ggtggaagtg cgatgagtct   360
ggtccgtgct tgcgcatctg gggcccaggc accctggtca ccgtctcctt agggcaacct   420
aa                                                                   422

<210> 508
<211> 411
<212> DNA
<213> Homo Sapiens

<220>
<221> misc_feature
<222> (1)...(411)
<223> n = A,T,C or G

<400> 508
atggagacag gcctcgctgg cttctcctgg tcgctgtgct caaaggtgtc cagtgtcagt    60
cggtggagga gtccgggggt cgcctggtca cgcctgggac acccctgaca ctcacctgca   120
cagtctctgg aatcgacctc agtagctact gcatgagctg ggtccgccag gctccaggga   180
aggggctgga atggatcgga atcattggta ctcctggtga cacatactac gcgaggtggg   240
cgaaaggccg attcaccatc tccaaaacct cgaccacggt gcatntgaaa atcnccagtc   300
cgacaaccga ggacacggcc acctatttct gtgccagaga tcttcgggat ggtagtagta   360
ctggttatta taaaatctgg ggcccaggca ccctggtcac cgtctccttg g            411

<210> 509
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 509
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1               5                   10                  15

<210> 510
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 510
Pro Glu Tyr Asn Arg Pro Leu Leu Ala Asn Asp Leu Met Leu Ile
1               5                   10                  15
```

```
        <210> 511
        <211> 15
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 511

Tyr His Pro Ser Met Phe Cys Ala Gly Gly Gly Gln Asp Gln Lys
1                 5                 10                15

        <210> 512
        <211> 15
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 512
Asp Ser Gly Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu
1                 5                 10                15

        <210> 513
        <211> 15
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 513
Ala Pro Cys Gly Gln Val Gly Val Pro Asx Val Tyr Thr Asn Leu
1                 5                 10                15

        <210> 514
        <211> 15
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 514
Leu Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
1                 5                 10                15

        <210> 515
        <211> 15
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab
```

<400> 515
Met Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg
1   5   10   15

<210> 516
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 516
Val Ser Glu Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln
1   5   10   15

<210> 517
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 517
Glu Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met
1   5   10   15

<210> 518
<211> 15
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 518
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg His Tyr Asp Glu Gly
1   5   10   15

<210> 519
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 519
Arg Ala Glu Pro Gly Thr Glu Ala Arg Arg Asn Tyr Asp Glu Gly Cys
1   5   10   15
Gly

<210> 520
<211> 25
<212> PRT
<213> Artificial Sequence

```
        <220>
        <223> Made in a lab

        <400> 520
Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly Thr
1               5                   10                  15
Glu Ala Arg Arg His Tyr Asp Glu Gly
            20              25


        <210> 521
        <211> 21
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 521
Ala Pro Phe Pro Asn Gly His Val Gly Ala Gly Gly Ser Gly Leu Leu
1               5                   10                  15
Pro Pro Pro Pro Ala
            20


        <210> 522
        <211> 20
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 522
Leu Leu Val Val Pro Ala Ile Lys Lys Asp Tyr Gly Ser Gln Glu Asp
1               5                   10                  15
Phe Thr Gln Val
            20


        <210> 523
        <211> 254
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <220>
        <221> VARIANT
        <222> (1)...(254)
        <223> Xaa = any amino acid

        <400> 523
Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
1               5                   10                  15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
            20                  25                  30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
        35                  40                  45
```

```
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
    50                      55                  60
Trp Val Leu Ser Ala Thr His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
65                      70                  75                  80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                85                  90                  95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
            100                 105                 110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
        115                 120                 125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
    130                 135                 140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
145                 150                 155                 160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
                165                 170                 175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
            180                 185                 190
Ala Gly Gly Gly Gln Xaa Gln Xaa Asp Ser Cys Asn Gly Asp Ser Gly
        195                 200                 205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
    210                 215                 220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
225                 230                 235                 240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
                245                 250
```

```
<210> 524
<211> 765
<212> DNA
<213> Homo sapien

<400> 524
atggccacag caggaaatcc ctggggctgg ttcctggggt acctcatcct tggtgtcgca    60
ggatcgctcg tctctggtag ctgcagccaa atcataaacg gcgaggactg cagcccgcac   120
tcgcagccct ggcaggcggc actggtcatg gaaaacgaat tgttctgctc gggcgtcctg   180
gtgcatccgc agtgggtgct gtcagccgca cactgtttcc agaactccta caccatcggg   240
ctgggcctgc acagtcttga ggccgaccaa gagccaggga ccagatggt ggaggccagc   300
ctctccgtac ggcacccaga gtacaacaga cccttgctcg ctaacgacct catgctcatc   360
aagttggacg aatccgtgtc cgagtctgac accatccgga gcatcagcat tgcttcgcag   420
tgccctaccg cggggaactc ttgcctcgtt tctggctggg gtctgctggc gaacggcaga   480
atgcctaccg tgctgcagtg cgtgaacgtg tcggtggtgt ctgaggaggt ctgcagtaag   540
ctctatgacc cgctgtacca ccccagcatg ttctgcgccg gcggagggca agaccagaag   600
gactcctgca cgggtgactc tggggggccc ctgatctgca cgggtactt gcagggcctt   660
gtgtctttcg gaaaagcccc gtgtggccaa gttggcgtgc caggtgtcta caccaacctc   720
tgcaaattca ctgagtggat agagaaaacc gtccaggcca gttaa                   765
```

```
<210> 525
<211> 254
<212> PRT
<213> Homo sapien

<400> 525
Met Ala Thr Ala Gly Asn Pro Trp Gly Trp Phe Leu Gly Tyr Leu Ile
1               5                   10                  15
Leu Gly Val Ala Gly Ser Leu Val Ser Gly Ser Cys Ser Gln Ile Ile
            20                  25                  30
Asn Gly Glu Asp Cys Ser Pro His Ser Gln Pro Trp Gln Ala Ala Leu
```

```
                35                      40                      45
Val Met Glu Asn Glu Leu Phe Cys Ser Gly Val Leu Val His Pro Gln
     50                      55                      60
Trp Val Leu Ser Ala Ala His Cys Phe Gln Asn Ser Tyr Thr Ile Gly
65                      70                      75                      80
Leu Gly Leu His Ser Leu Glu Ala Asp Gln Glu Pro Gly Ser Gln Met
                85                      90                      95
Val Glu Ala Ser Leu Ser Val Arg His Pro Glu Tyr Asn Arg Pro Leu
             100                     105                     110
Leu Ala Asn Asp Leu Met Leu Ile Lys Leu Asp Glu Ser Val Ser Glu
             115                     120                     125
Ser Asp Thr Ile Arg Ser Ile Ser Ile Ala Ser Gln Cys Pro Thr Ala
     130                     135                     140
Gly Asn Ser Cys Leu Val Ser Gly Trp Gly Leu Leu Ala Asn Gly Arg
145                     150                     155                     160
Met Pro Thr Val Leu Gln Cys Val Asn Val Ser Val Val Ser Glu Glu
             165                     170                     175
Val Cys Ser Lys Leu Tyr Asp Pro Leu Tyr His Pro Ser Met Phe Cys
             180                     185                     190
Ala Gly Gly Gly Gln Asp Gln Lys Asp Ser Cys Asn Gly Asp Ser Gly
             195                     200                     205
Gly Pro Leu Ile Cys Asn Gly Tyr Leu Gln Gly Leu Val Ser Phe Gly
     210                     215                     220
Lys Ala Pro Cys Gly Gln Val Gly Val Pro Gly Val Tyr Thr Asn Leu
225                     230                     235                     240
Cys Lys Phe Thr Glu Trp Ile Glu Lys Thr Val Gln Ala Ser
             245                     250
```

<210> 526
<211> 963
<212> DNA
<213> Homo sapiens

<400> 526
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atgagttcct gcaacttcac acatgccacc tttgtgctta ttggtatccc aggattagag 60
aaagcccatt tctgggttgg cttccccctc ctttccatgt atgtagtggc aatgtttgga 120
aactgcatcg tggtcttcat cgtaaggacg gaacgcagcc tgcacgctcc gatgtacctc 180
tttctctgca tgcttgcagc cattgacctg gccttatcca catccaccat gcctaagatc 240
cttgcccttt tctggtttga ttcccgagag attagctttg aggcctgtct tacccagatg 300
ttctttattc atgccctctc agccattgaa tccaccatcc tgctggccat ggcctttgac 360
cgttatgtgg ccatctgcca cccactcgcg catgctgcag tgctcaacaa tacagtaaca 420
gcccagattg catcgtggc tgtggtccgc ggatccctct ttttttttccc actgcctctg 480
ctgatcaagc ggctggcctt ctgccactcc aatgtcctct cgcactccta ttgtgtccac 540
caggatgtaa tgaagttggc ctatgcagac actttgccca atgtggtata tggtcttact 600
gccattctgc tggtcatggg cgtggacgta atgttcatct ccttgtccta ttttctgata 660
atacgaacgg ttctgcaact gccttccaag tcagagcggg ccaaggcctt tggaacctgt 720
gtgtcacaca ttggtgtggt actcgccttc tatgtgccac ttattggcct ctcagttgta 780
caccgctttg gaaacagcct tcatcccatt gtgcgtgttg tcatgggtga catctacctg 840
ctgctgcctc ctgtcatcaa tcccatcatc tatggtgcca aaaccaaaca gatcagaaca 900
cgggtgctgg ctatgttcaa gatcagctgt gacaaggact gcaggctgt gggaggcaag 960
tga                                                                  963
```

<210> 527
<211> 320
<212> PRT
<213> Homo sapiens

<400> 527

Met Ser Ser Cys Asn Phe Thr His Ala Thr Phe Val Leu Ile Gly Ile
                      5   10   15

Pro Gly Leu Glu Lys Ala His Phe Trp Val Gly Phe Pro Leu Leu Ser
              20   25   30

Met Tyr Val Val Ala Met Phe Gly Asn Cys Ile Val Val Phe Ile Val
              35   40   45

Arg Thr Glu Arg Ser Leu His Ala Pro Met Tyr Leu Phe Leu Cys Met
    50   55   60

Leu Ala Ala Ile Asp Leu Ala Leu Ser Thr Ser Thr Met Pro Lys Ile
65   70   75   80

Leu Ala Leu Phe Trp Phe Asp Ser Arg Glu Ile Ser Phe Glu Ala Cys
                85   90   95

Leu Thr Gln Met Phe Phe Ile His Ala Leu Ser Ala Ile Glu Ser Thr
              100   105   110

Ile Leu Leu Ala Met Ala Phe Asp Arg Tyr Val Ala Ile Cys His Pro
        115   120   125

Leu Arg His Ala Ala Val Leu Asn Asn Thr Val Thr Ala Gln Ile Gly
    130   135   140

Ile Val Ala Val Val Arg Gly Ser Leu Phe Phe Phe Pro Leu Pro Leu
145   150   155   160

Leu Ile Lys Arg Leu Ala Phe Cys His Ser Asn Val Leu Ser His Ser
                165   170   175

Tyr Cys Val His Gln Asp Val Met Lys Leu Ala Tyr Ala Asp Thr Leu
        180   185   190

Pro Asn Val Val Tyr Gly Leu Thr Ala Ile Leu Leu Val Met Gly Val
        195   200   205

Asp Val Met Phe Ile Ser Leu Ser Tyr Phe Leu Ile Ile Arg Thr Val
    210   215   220

Leu Gln Leu Pro Ser Lys Ser Glu Arg Ala Lys Ala Phe Gly Thr Cys
225   230   235   240

Val Ser His Ile Gly Val Val Leu Ala Phe Tyr Val Pro Leu Ile Gly
              245   250   255

Leu Ser Val Val His Arg Phe Gly Asn Ser Leu His Pro Ile Val Arg
              260   265   270

Val Val Met Gly Asp Ile Tyr Leu Leu Leu Pro Pro Val Ile Asn Pro
    275   280   285

Ile Ile Tyr Gly Ala Lys Thr Lys Gln Ile Arg Thr Arg Val Leu Ala
    290   295   300

Met Phe Lys Ile Ser Cys Asp Lys Asp Leu Gln Ala Val Gly Gly Lys

305   310   315   320

```
        <210> 528
        <211> 20
        <212> DNA
        <213> Homo Sapien

        <400> 528
actatggtcc agaggctgtg                                              20

        <210> 529
        <211> 20
        <212> DNA
        <213> Homo Sapien

        <400> 529
atcacctatg tgccgcctct                                              20

<210> 530
<211> 1852
<212> DNA
<213> Homo sapiens

<400> 530
ggcacgagaa ttaaaaccct cagcaaaaca ggcatagaag ggacatacct taaagtaata 60
aaaaccacct atgacaagcc cacagccaac ataatactaa atggggaaaa gttagaagca 120
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<210> 531
<211> 879
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<212> DNA
<213> Homo sapiens

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tgcaagtggt gctgccactg cttcccctgc tgcaggggga gcggcaagag caacgtggtc 180
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<210> 532
<211> 292
<212> PRT
<213> Homo sapiens

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Met His Leu Ser Phe Pro Ala Phe Leu Pro Pro Trp Met Asp Arg Gly
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            20                  25                  30

Val Lys Thr Leu Gly Ser Lys Arg Cys Lys Trp Cys Cys His Cys Phe
        35                  40                  45

Pro Cys Cys Arg Gly Ser Gly Lys Ser Asn Val Val Ala Trp Gly Asp
    50                  55                  60

Tyr Asp Asp Ser Ala Phe Met Asp Pro Arg Tyr His Val His Gly Glu
65                  70                  75                  80

Asp Leu Asp Lys Leu His Arg Ala Ala Trp Trp Gly Lys Val Pro Arg
                85                  90                  95

Lys Asp Leu Ile Val Met Leu Arg Asp Thr Asp Val Asn Lys Arg Asp
            100                 105                 110

Lys Gln Lys Arg Thr Ala Leu His Leu Ala Ser Ala Asn Gly Asn Ser
        115                 120                 125

Glu Val Val Lys Leu Val Leu Asp Arg Arg Cys Gln Leu Asn Val Leu
    130                 135                 140

Asp Asn Lys Lys Arg Thr Ala Leu Thr Lys Ala Val Gln Cys Gln Glu
145                 150                 155                 160

Asp Glu Cys Ala Leu Met Leu Leu Glu His Gly Thr Asp Pro Asn Ile
                165                 170                 175
```

Pro Asp Glu Tyr Gly Asn Thr Thr Leu His Tyr Ala Val Tyr Asn Glu
        180   185   190

Asp Lys Leu Met Ala Lys Ala Leu Leu Leu Tyr Gly Ala Asp Ile Glu
        195   200   205

Ser Lys Asn Lys His Gly Leu Thr Pro Leu Leu Leu Gly Ile His Glu
    210   215   220

Gln Lys Gln Gln Val Val Lys Phe Leu Ile Lys Lys Lys Ala Asn Leu
225   230   235   240

Asn Ala Leu Asp Arg Tyr Gly Arg Thr Ala Leu Ile Leu Ala Val Cys
                245   250   255

Cys Gly Ser Ala Ser Ile Val Ser Pro Leu Leu Glu Gln Asn Val Asp
        260   265   270

Val Ser Ser Gln Asp Leu Glu Arg Arg Pro Glu Ser Met Leu Phe Leu
        275   280   285

Val Ile Ile Met
        290

<210> 533
<211> 801
<212> DNA
<213> Homo sapiens

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<210> 534
<211> 266
<212> PRT
<213> Homo sapiens

<400> 534
Met Tyr Lys Leu Gln Cys Asn Asn Cys Ala Thr Asn Gly Ala Thr Glu
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Arg Lys Gln Ala Ala Gly Ser Gly Ala Gly Tyr Ala Leu Pro Ser Ala
        20   25   30

```
Leu Gln Ser Met Pro Gln Gly Ser Tyr Ala Thr Ala Arg Phe Leu Val
        35              40              45
```

```
Ala Lys Arg Pro Thr Thr Gly His Leu Glu Lys Glu Phe Met Phe His
        50              55              60
```

```
Cys Arg Lys Gln Pro Gly Ser Pro Ser Arg Gly Leu Gly Leu Leu Trp
65              70              75              80
```

```
Pro Trp Pro Asp Ile Glu Phe Val Pro Arg Gln Asp Lys Leu Thr Gln
                85              90              95
```

```
Ser Ser Val Leu Val Pro Gln Ile Cys Ala Cys Gln Thr Arg Pro Asn
            100             105             110
```

```
Trp Leu Asn Glu Gln Pro Ala Thr Ser Ala Gly Val Arg Leu Glu Glu
        115             120             125
```

```
Val Asp Gln Pro Pro Thr Leu Pro Ser Gln Gly Ser Gly Trp Pro Cys
    130             135             140
```

```
Ser His Ser Leu Ser Gly Cys His Leu Met Ala Asp Ile Ala Lys Ala
145             150             155             160
```

```
Leu Gly Lys Ala Asp Gly Pro Trp Pro Tyr Leu Phe Val Arg Arg Thr
                165             170             175
```

```
Asp Val Pro Cys Pro Ala Ala Ser Glu Val Gly Gly Cys Ala Pro Ser
            180             185             190
```

```
Ser Trp His Thr Leu Ala Glu Val Thr Gly Cys Ser Leu Ser Pro Leu
        195             200             205
```

```
Ser Leu Ala Gln His Ala Gln Ala Ser Val Leu Leu Leu Cys Tyr Lys
    210             215             220
```

```
Trp Ser His Ile Gly Glu Thr Ser Ser His Leu Arg Ser Lys Val Tyr
225             230             235             240
```

```
Ala Ala Phe Gly Gly Ser Ser Pro Cys Leu Lys Gly Leu Met Ser Leu
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```

```
Trp Ala Ser Trp Leu Pro Arg Gly Arg Pro
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```

```
<210> 535
<211> 6082
<212> DNA
<213> Homo sapiens
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gcaagatgct gcccgtgtac caggaggtga agcccaaccc gctgcaggac gcgaacctct 240
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<210> 536
<211> 6140
<212> DNA
<213> Homo sapiens

<220>
<221> unsure
<222> (4535)
<223> n=A,T,C or G

<400> 536
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<210> 537
<211> 1228
<212> PRT
<213> Homo sapiens

<400> 537
Met Leu Pro Val Tyr Gln Glu Val Lys Pro Asn Pro Leu Gln Asp Ala
                  5   10   15

Asn Leu Cys Ser Arg Val Phe Phe Trp Trp Leu Asn Pro Leu Phe Lys
               20   25   30

Ile Gly His Lys Arg Arg Leu Glu Glu Asp Asp Met Tyr Ser Val Leu
        35   40   45

Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu Leu Gln Gly Phe Trp
   50   55   60

Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala Gln Lys Pro Ser Leu

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            65                      70                      75                      80

        Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser Tyr Leu Val Leu Gly
                        85                      90                      95

        Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val Ile Gln Pro Ile Phe
                       100                     105                     110

        Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr Asp Pro Met Asp Ser
                       115                     120                     125

        Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr Val Leu Thr Phe Cys
                130                     135                     140

        Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr Phe Tyr His Val Gln
        145                     150                     155                     160

        Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys His Met Ile Tyr Arg
                        165                     170                     175

        Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly Lys Thr Thr Thr Gly
                        180                     185                     190

        Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn Lys Phe Asp Gln Val
                       195                     200                     205

        Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro Leu Gln Ala Ile Ala
                210                     215                     220

        Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile Ser Cys Leu Ala Gly
        225                     230                     235                     240

        Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln Ser Cys Phe Gly Lys
                        245                     250                     255

        Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr Phe Thr Asp Ala Arg
                        260                     265                     270

        Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile Arg Ile Ile Lys Met
                        275                     280                     285

        Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile Thr Asn Leu Arg Lys
                290                     295                     300

        Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys Leu Arg Gly Met Asn
        305                     310                     315                     320

        Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile Val Phe Val Thr Phe
                        325                     330                     335

        Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr Ala Ser Arg Val Phe
                        340                     345                     350

        Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu Thr Val Thr Leu Phe
                        355                     360                     365

        Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala Ile Val Ser Ile Arg
                370                     375                     380
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Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile Ser Gln Arg Asn Arg
385   390   395   400

Gln Leu Pro Ser Asp Gly Lys Lys Met Val His Val Gln Asp Phe Thr
                405   410   415

Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr Leu Gln Gly Leu Ser
                420   425   430

Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val Val Gly Pro Val Gly
        435   440   445

Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu Gly Glu Leu Ala Pro
    450   455   460

Ser His Gly Leu Val Ser Val His Gly Arg Ile Ala Tyr Val Ser Gln
465   470   475   480

Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser Asn Ile Leu Phe Gly
                485   490   495

Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val Ile Lys Ala Cys Ala
            500   505   510

Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly Asp Leu Thr Val Ile
        515   520   525

Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln Lys Ala Arg Val Asn
    530   535   540

Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile Tyr Leu Leu Asp Asp
545   550   555   560

Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg His Leu Phe Glu Leu
                565   570   575

Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr Ile Leu Val Thr His
            580   585   590

Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile Leu Ile Leu Lys Asp
        595   600   605

Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu Phe Leu Lys Ser Gly
    610   615   620

Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn Glu Glu Ser Glu Gln
625   630   635   640

Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn Arg Thr Phe Ser Glu
                645   650   655

Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro Ser Leu Lys Asp Gly
            660   665   670

Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro Val Thr Leu Ser Glu
        675   680   685

Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln Ala Tyr Lys Asn Tyr
    690   695   700

Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile Phe Leu Ile Leu Leu
705   710   715   720

Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln Asp Trp Trp Leu Ser
            725   730   735

Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val Thr Val Asn Gly Gly
        740   745   750

Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp Tyr Leu Gly Ile Tyr
        755   760   765

Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly Ile Ala Arg Ser Leu
    770   775   780

Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln Thr Leu His Asn Lys
785   790   795   800

Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu Phe Phe Asp Arg Asn
            805   810   815

Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys Asp Ile Gly His Leu
            820   825   830

Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe Ile Gln Thr Leu Leu
        835   840   845

Gln Val Val Gly Val Val Ser Val Ala Val Ala Val Ile Pro Trp Ile
    850   855   860

Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe Ile Phe Leu Arg Arg
865   870   875   880

Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg Leu Glu Ser Thr Thr
            885   890   895

Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser Leu Gln Gly Leu Trp
            900   905   910

Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys Gln Glu Leu Phe Asp
        915   920   925

Ala His Gln Asp Leu His Ser Glu Ala Trp Phe Leu Phe Leu Thr Thr
    930   935   940

Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile Cys Ala Met Phe Val
945   950   955   960

Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala Lys Thr Leu Asp Ala
            965   970   975

Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu Thr Leu Met Gly Met
        980   985   990

Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val Glu Asn Met Met Ile

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                  995                      1000                    1005

Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu Glu Lys Glu Ala Pro
          1010                1015                1020

Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp Pro His Glu Gly Val
1025                1030                1035                1040

Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser Pro Gly Gly Pro Leu
                1045                1050                1055

Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser Gln Glu Lys Val Gly
                1060                1065                1070

Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Ile Ser Ala Leu
              1075                1080                1085

Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp Ile Asp Lys Ile Leu
          1090                1095                1100

Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys Lys Met Ser Ile Ile
1105                1110                1115                1120

Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met Arg Lys Asn Leu Asp
                1125                1130                1135

Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp Asn Ala Leu Gln Glu
              1140                1145                1150

Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro Gly Lys Met Asp Thr
          1155                1160                1165

Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val Gly Gln Arg Gln Leu
          1170                1175                1180

Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn Gln Ile Leu Ile Ile
1185                1190                1195                1200

Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr Asp Glu Leu Ile Gln
              1205                1210                1215

Lys Lys Ser Gly Arg Asn Leu Pro Thr Ala Pro Cys
          1220                1225
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<210> 538
<211> 1261
<212> PRT
<213> Homo sapiens

<400> 538
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Met Tyr Ser Val Leu Pro Glu Asp Arg Ser Gln His Leu Gly Glu Glu
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Leu Gln Gly Phe Trp Asp Lys Glu Val Leu Arg Ala Glu Asn Asp Ala
              20              25                  30

Gln Lys Pro Ser Leu Thr Arg Ala Ile Ile Lys Cys Tyr Trp Lys Ser
          35              40                  45
```

Tyr Leu Val Leu Gly Ile Phe Thr Leu Ile Glu Glu Ser Ala Lys Val
    50   55   60

Ile Gln Pro Ile Phe Leu Gly Lys Ile Ile Asn Tyr Phe Glu Asn Tyr
65   70   75   80

Asp Pro Met Asp Ser Val Ala Leu Asn Thr Ala Tyr Ala Tyr Ala Thr
          85   90   95

Val Leu Thr Phe Cys Thr Leu Ile Leu Ala Ile Leu His His Leu Tyr
       100   105   110

Phe Tyr His Val Gln Cys Ala Gly Met Arg Leu Arg Val Ala Met Cys
    115   120   125

His Met Ile Tyr Arg Lys Ala Leu Arg Leu Ser Asn Met Ala Met Gly
    130   135   140

Lys Thr Thr Thr Gly Gln Ile Val Asn Leu Leu Ser Asn Asp Val Asn
145   150   155   160

Lys Phe Asp Gln Val Thr Val Phe Leu His Phe Leu Trp Ala Gly Pro
         165   170   175

Leu Gln Ala Ile Ala Val Thr Ala Leu Leu Trp Met Glu Ile Gly Ile
         180   185   190

Ser Cys Leu Ala Gly Met Ala Val Leu Ile Ile Leu Leu Pro Leu Gln
       195   200   205

Ser Cys Phe Gly Lys Leu Phe Ser Ser Leu Arg Ser Lys Thr Ala Thr
    210   215   220

Phe Thr Asp Ala Arg Ile Arg Thr Met Asn Glu Val Ile Thr Gly Ile
225   230   235   240

Arg Ile Ile Lys Met Tyr Ala Trp Glu Lys Ser Phe Ser Asn Leu Ile
         245   250   255

Thr Asn Leu Arg Lys Lys Glu Ile Ser Lys Ile Leu Arg Ser Ser Cys
       260   265   270

Leu Arg Gly Met Asn Leu Ala Ser Phe Phe Ser Ala Ser Lys Ile Ile
       275   280   285

Val Phe Val Thr Phe Thr Thr Tyr Val Leu Leu Gly Ser Val Ile Thr
    290   295   300

Ala Ser Arg Val Phe Val Ala Val Thr Leu Tyr Gly Ala Val Arg Leu
305   310   315   320

Thr Val Thr Leu Phe Phe Pro Ser Ala Ile Glu Arg Val Ser Glu Ala
         325   330   335

Ile Val Ser Ile Arg Arg Ile Gln Thr Phe Leu Leu Leu Asp Glu Ile
       340   345   350

Ser Gln Arg Asn Arg Gln Leu Pro Ser Asp Gly Lys Lys Met Val His
        355   360   365

Val Gln Asp Phe Thr Ala Phe Trp Asp Lys Ala Ser Glu Thr Pro Thr
    370   375   380

Leu Gln Gly Leu Ser Phe Thr Val Arg Pro Gly Glu Leu Leu Ala Val
385   390   395   400

Val Gly Pro Val Gly Ala Gly Lys Ser Ser Leu Leu Ser Ala Val Leu
                405   410   415

Gly Glu Leu Ala Pro Ser His Gly Leu Val Ser Val His Gly Arg Ile
            420   425   430

Ala Tyr Val Ser Gln Gln Pro Trp Val Phe Ser Gly Thr Leu Arg Ser
        435   440   445

Asn Ile Leu Phe Gly Lys Lys Tyr Glu Lys Glu Arg Tyr Glu Lys Val
    450   455   460

Ile Lys Ala Cys Ala Leu Lys Lys Asp Leu Gln Leu Leu Glu Asp Gly
465   470   475   480

Asp Leu Thr Val Ile Gly Asp Arg Gly Thr Thr Leu Ser Gly Gly Gln
                485   490   495

Lys Ala Arg Val Asn Leu Ala Arg Ala Val Tyr Gln Asp Ala Asp Ile
            500   505   510

Tyr Leu Leu Asp Asp Pro Leu Ser Ala Val Asp Ala Glu Val Ser Arg
    515   520   525

His Leu Phe Glu Leu Cys Ile Cys Gln Ile Leu His Glu Lys Ile Thr
    530   535   540

Ile Leu Val Thr His Gln Leu Gln Tyr Leu Lys Ala Ala Ser Gln Ile
545   550   555   560

Leu Ile Leu Lys Asp Gly Lys Met Val Gln Lys Gly Thr Tyr Thr Glu
            565   570   575

Phe Leu Lys Ser Gly Ile Asp Phe Gly Ser Leu Leu Lys Lys Asp Asn
        580   585   590

Glu Glu Ser Glu Gln Pro Pro Val Pro Gly Thr Pro Thr Leu Arg Asn
        595   600   605

Arg Thr Phe Ser Glu Ser Ser Val Trp Ser Gln Gln Ser Ser Arg Pro
    610   615   620

Ser Leu Lys Asp Gly Ala Leu Glu Ser Gln Asp Thr Glu Asn Val Pro
625   630   635   640

Val Thr Leu Ser Glu Glu Asn Arg Ser Glu Gly Lys Val Gly Phe Gln
                645   650   655

Ala Tyr Lys Asn Tyr Phe Arg Ala Gly Ala His Trp Ile Val Phe Ile

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                    660                    665                    670

Phe Leu Ile Leu Leu Asn Thr Ala Ala Gln Val Ala Tyr Val Leu Gln
        675                680                685

Asp Trp Trp Leu Ser Tyr Trp Ala Asn Lys Gln Ser Met Leu Asn Val
    690                695                700

Thr Val Asn Gly Gly Gly Asn Val Thr Glu Lys Leu Asp Leu Asn Trp
705                710                715                720

Tyr Leu Gly Ile Tyr Ser Gly Leu Thr Val Ala Thr Val Leu Phe Gly
                725                730                735

Ile Ala Arg Ser Leu Leu Val Phe Tyr Val Leu Val Asn Ser Ser Gln
            740                745                750

Thr Leu His Asn Lys Met Phe Glu Ser Ile Leu Lys Ala Pro Val Leu
        755                760                765

Phe Phe Asp Arg Asn Pro Ile Gly Arg Ile Leu Asn Arg Phe Ser Lys
    770                775                780

Asp Ile Gly His Leu Asp Asp Leu Leu Pro Leu Thr Phe Leu Asp Phe
785                790                795                800

Ile Gln Thr Leu Leu Gln Val Val Gly Val Val Ser Val Ala Val Ala
            805                810                815

Val Ile Pro Trp Ile Ala Ile Pro Leu Val Pro Leu Gly Ile Ile Phe
            820                825                830

Ile Phe Leu Arg Arg Tyr Phe Leu Glu Thr Ser Arg Asp Val Lys Arg
        835                840                845

Leu Glu Ser Thr Thr Arg Ser Pro Val Phe Ser His Leu Ser Ser Ser
    850                855                860

Leu Gln Gly Leu Trp Thr Ile Arg Ala Tyr Lys Ala Glu Glu Arg Cys
865                870                875                880

Gln Glu Leu Phe Asp Ala His Gln Asp Leu His Ser Glu Ala Trp Phe
            885                890                895

Leu Phe Leu Thr Thr Ser Arg Trp Phe Ala Val Arg Leu Asp Ala Ile
        900                905                910

Cys Ala Met Phe Val Ile Ile Val Ala Phe Gly Ser Leu Ile Leu Ala
        915                920                925

Lys Thr Leu Asp Ala Gly Gln Val Gly Leu Ala Leu Ser Tyr Ala Leu
    930                935                940

Thr Leu Met Gly Met Phe Gln Trp Cys Val Arg Gln Ser Ala Glu Val
945                950                955                960

Glu Asn Met Met Ile Ser Val Glu Arg Val Ile Glu Tyr Thr Asp Leu
            965                970                975
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Glu Lys Glu Ala Pro Trp Glu Tyr Gln Lys Arg Pro Pro Pro Ala Trp
        980                     985                 990

Pro His Glu Gly Val Ile Ile Phe Asp Asn Val Asn Phe Met Tyr Ser
        995                     1000                1005

Pro Gly Gly Pro Leu Val Leu Lys His Leu Thr Ala Leu Ile Lys Ser
        1010                    1015                1020

Gln Glu Lys Val Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser
1025                    1030                    1035                1040

Leu Ile Ser Ala Leu Phe Arg Leu Ser Glu Pro Glu Gly Lys Ile Trp
                1045                    1050                    1055

Ile Asp Lys Ile Leu Thr Thr Glu Ile Gly Leu His Asp Leu Arg Lys
        1060                    1065                    1070

Lys Met Ser Ile Ile Pro Gln Glu Pro Val Leu Phe Thr Gly Thr Met
        1075                    1080                    1085

Arg Lys Asn Leu Asp Pro Phe Asn Glu His Thr Asp Glu Glu Leu Trp
        1090                    1095                    1100

Asn Ala Leu Gln Glu Val Gln Leu Lys Glu Thr Ile Glu Asp Leu Pro
1105                    1110                    1115                1120

Gly Lys Met Asp Thr Glu Leu Ala Glu Ser Gly Ser Asn Phe Ser Val
                1125                    1130                    1135

Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala Ile Leu Arg Lys Asn
                1140                    1145                    1150

Gln Ile Leu Ile Ile Asp Glu Ala Thr Ala Asn Val Asp Pro Arg Thr
        1155                    1160                    1165

Asp Glu Leu Ile Gln Lys Lys Ile Arg Glu Lys Phe Ala His Cys Thr
        1170                    1175                    1180

Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Ile Asp Ser Asp Lys
1185                    1190                    1195                1200

Ile Met Val Leu Asp Ser Gly Arg Leu Lys Glu Tyr Asp Glu Pro Tyr
                1205                    1210                    1215

Val Leu Leu Gln Asn Lys Glu Ser Leu Phe Tyr Lys Met Val Gln Gln
                1220                    1225                    1230

Leu Gly Lys Ala Glu Ala Ala Ala Leu Thr Glu Thr Ala Lys Gln Arg
        1235                    1240                    1245

Trp Gly Phe Thr Met Leu Ala Arg Leu Val Ser Asn Ser
        1250                    1255                    1260
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<210> 539
<211> 10
<212> PRT

<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 539
Cys Leu Ser His Ser Val Ala Val Val Thr
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<210> 540
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> Made in a lab

<400> 540
Ala Val Val Thr Ala Ser Ala Ala Leu
1   5

<210> 541
<211> 14
<212> PRT
<213> Homo sapiens

<400> 541
Leu Ala Gly Leu Leu Cys Pro Asp Pro Arg Pro Leu Glu Leu
                5   10

<210> 542
<211> 15
<212> PRT
<213> Homo sapiens

<400> 542
Thr Gln Val Val Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
                5   10   15

<210> 543
<211> 12
<212> PRT
<213> Homo sapiens

<400> 543
Phe Met Gly Ser Ile Val Gln Leu Ser Gln Ser Val
                5   10

<210> 544
<211> 18
<212> PRT
<213> Homo sapiens

<400> 544
Thr Tyr Val Pro Pro Leu Leu Leu Glu Val Gly Val Glu Glu Lys Phe

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                     5                10                15

Met Thr



<210> 545
<211> 18
<212> PRT
<213> Homo sapiens

<400> 545
Met Asp Arg Leu Val Gln Arg Phe Gly Thr Arg Ala Val Tyr Leu Ala
                 5                10                15

Ser Val



<210> 546
<211> 29
<212> PRT
<213> Homo sapiens

<400> 546
Phe Val Gly Glu Gly Leu Tyr Gln Gly Val Pro Arg Ala Glu Pro Gly
                 5                10                15

Thr Glu Ala Arg Arg His Tyr Asp Glu Gly Val Arg Met
             20                25



<210> 547
<211> 58
<212> PRT
<213> Homo sapiens

<400> 547
Val Ala Glu Glu Ala Ala Leu Gly Pro Thr Glu Pro Ala Glu Gly Leu
                 5                10                15

Ser Ala Pro Ser Leu Ser Pro His Cys Cys Pro Cys Arg Ala Arg Leu
             20                25                30

Ala Phe Arg Asn Leu Gly Ala Leu Leu Pro Arg Leu His Gln Leu Cys
             35                40                45

Cys Arg Met Pro Arg Thr Leu Arg Arg Leu
         50                55



<210> 548
<211> 18
<212> PRT
<213> Homo sapiens

<400> 548
Ile Asp Trp Asp Thr Ser Ala Leu Ala Pro Tyr Leu Gly Thr Gln Glu
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200

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                         5                    10                    15

Glu Cys


<210> 549
<211> 18
<212> PRT
<213> Homo sapiens

<400> 549
Leu Glu Ala Leu Leu Ser Asp Leu Phe Arg Asp Pro Asp His Cys Arg
                    5                    10                    15

Gln Ala


<210> 550
<211> 14
<212> PRT
<213> Homo sapiens

<400> 550
Ser Asp His Trp Arg Gly Arg Tyr Gly Arg Arg Arg Pro Phe
                    5                    10


        <210> 551
        <211> 11
        <212> PRT
        <213> Artificial Sequence

        <220>
        <223> Made in a lab

        <400> 551
 Phe Asp Lys Ser Asp Leu Ala Lys Tyr Ser Ala
  1             5                    10
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